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Quinoxyfen

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Overview

Registration Decision for Compound Quinoxyfen

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, has granted conditional registration for the sale and use of Quinoxyfen Technical Fungicide and Quintec Fungicide, containing the technical grade active ingredient quinoxyfen, to control powdery mildew on several fruits and vegetables.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

Although the risks and value have been found acceptable when all risk reduction measures are followed, the applicant must submit additional scientific information as a condition of registration.

This Overview describes the key points of the evaluation, while the Science Evaluation Section provides detailed technical information on the human health, environmental and value assessments of quinoxyfen and Quintec Fungicide.

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[1] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its proposed conditions of registration. The Act also requires that products have value[2] when used according to the label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (for example, children) as well as organisms in the environment (for example, those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides and Pest Management Portion of the Health Canada website at healthcanada.gc.ca/pmra.

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1 "Acceptable risks" as defined by subsection 2(2) of the *Pest Control Products Act*.

2 "Value" as defined by subsection 2(1) of the *Pest Control Products Act*: "the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (*a*) efficacy; (*b*) effect on host organisms in connection with which it is intended to be used; and (*c*) health, safety and environmental benefits and social and economic impact."

What Is Quinoxyfen?

Quinoxyfen is the active ingredient in the end-use product Quintec Fungicide. This protectant fungicide is to be used in Canada for the control of powdery mildew on stone fruits, grapes, strawberry, melon, squash, pumpkin, lettuce and hops.

Health Considerations

Can Approved Uses of Quinoxyfen Affect Human Health?

Quinoxyfen is unlikely to affect your health when used according to label directions.

Potential exposure to quinoxyfen may occur through the diet (food and water) or when handling and applying the product. When assessing health risks, two key factors are considered: the levels where no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose where no effects are observed. The health effects noted in animals occur at doses more than 100-times higher (and often much higher) than levels to which humans are normally exposed when quinoxyfen products are used according to label directions.

Quinoxyfen Technical Fungicide was of low toxicity by the oral, dermal and inhalation routes of exposure in rats. It was mildly irritating to the eyes and non-irritating to the skin of rabbits. Quinoxyfen was considered to be a dermal sensitizer according to the Maximization test method. Consequently, the signal words "CAUTION – EYE IRRITANT" and "POTENTIAL SKIN SENSITIZER" are required on the label.

The end-use product Quintec Fungicide was of low toxicity when given as a single oral, dermal and inhalation dose to rats, and was minimally irritating to the eyes and slightly irritating to the skin of rabbits. It was not a skin sensitizer in guinea pigs. Consequently, no signal words are required on the label.

Quinoxyfen did not cause cancer in animals, was not genotoxic and did not cause birth defects in the developing young. There was also no indication that quinoxyfen caused damage to the nervous system and there were no adverse effects on reproduction. The first signs of toxicity in animals given daily doses of quinoxyfen over longer periods of time were effects on body weight and the liver. Observations in dogs at high doses included effects on red blood cells (anemia).

When quinoxyfen was given to pregnant animals, increased abortions were only observed at doses that were toxic to the mother, indicating that the fetus is not more sensitive to quinoxyfen than the adult animal.

The risk assessment protects against these effects by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

Residues in Water and Food

Dietary risks from food and water are not of concern.

Aggregate dietary intake estimates (food plus water) revealed that the general population and children one to two years old, the subpopulation which would ingest the most quinoxyfen relative to body weight, are expected to be exposed to less than 2.1% of the acceptable daily intake. Based on these estimates, the chronic dietary risk from quinoxyfen is not of concern for all segments of the population. Quinoxyfen is not carcinogenic; therefore, a chronic cancer dietary exposure assessment is not required.

Animal studies revealed no acute health effects. A single dose of quinoxyfen is not likely to cause acute health effects in the general population (including infants and children). An acute reference dose was not established, therefore an acute dietary intake estimate is not required.

The *Food and Drugs Act* prohibits the sale of adulterated food, that is, food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act*. Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

Residue trials conducted throughout Canada and the United States using quinoxyfen on cantaloupes, cherries, grapes, hops, lettuce, peaches, plums, strawberries and winter squash were acceptable. The MRLs for this active ingredient can be found in the Science Evaluation section of this Evaluation Report.

Occupational Risks from Handling Quintec Fungicide

Occupational risks are not of concern when Quintec Fungicide is used according to the label directions, which include protective measures.

Farmers and custom applicators who mix, load or apply Quintec Fungicide as well as field workers re-entering freshly treated fields can come in direct contact with Quintec Fungicide residues on the skin. Therefore, the label specifies that anyone mixing/loading and applying Quintec Fungicide must wear a long sleeved shirt, long pants, shoes plus socks and chemical resistant gloves. As an extra precaution, workers that handle the concentrated product are advised to wear coveralls, chemical resistant gloves, goggles and rubber boots. The label also requires that workers do not enter treated fields for 12 hours after application. Taking into consideration these label statements, the number of applications and the expectation of the exposure period for handlers and workers, the risk to these individuals are not a concern.

For bystanders, exposure is expected to be much less than that for workers and is considered negligible. Therefore, health risks to bystanders are not of concern.

Environmental Considerations

What Happens When Quinoxyfen Is Introduced Into the Environment?

Quinoxyfen can pose a risk to freshwater and estuarine fish, invertebrates and algae; therefore, label statements and spray buffer zones are required to protect these organisms and to minimize exposure to the aquatic environment. Additional data will be requested to address uncertainties with regard to the chronic risk to aquatic organisms and the bioaccumulation potential of the major transformation product of quinoxyfen: 2-oxo-quinoxyfen.

Quinoxyfen has the potential to enter into the environment when applied as a fungicide to field crops. Quinoxyfen has low water solubility and abiotic transformation processes, such as hydrolysis and phototransformation, are not an important route of dissipation of quinoxyfen in the environment. Quinoxyfen has a low volatility indicating that long-range atmospheric transport is unlikely. Quinoxyfen is moderately persistent to persistent in terrestrial environments, but is non-persistent to slightly persistent in water. The major transformation product 2-oxo-quinoxyfen is formed in soil and water and its persistence in both media is unknown. The major transformation product DCHQ is formed in soil, particularly under acidic conditions. Laboratory and modelling data show that quinoxyfen and 2-oxo-quinoxyfen are not expected to be mobile in soil and have a low potential to leach. In aquatic systems, quinoxyfen is expected to partition to sediment. A terrestrial field study conducted in Canada indicates that quinoxyfen is moderately persistent and tends to stay in the upper soil layer, as do the major transformation products 2-oxo-quinoxyfen and DCHQ. Monitoring studies conducted in Europe show little dissipation of quinoxyfen from soil over winter, indicating that quinoxyfen can be persistent under field conditions.

Laboratory studies indicate that quinoxyfen has the potential to bioaccumulate. Under field conditions, residues were quantified in terrestrial and aquatic biota. Low levels of bioaccumulation have been observed in terrestrial biota. In aquatic biota, bioaccumulation could not be assessed given the lack of data on water concentrations and non-detected concentrations in sediment. Additional data have been requested to further characterise the fate and bioaccumulation potential of the 2-oxo-quinoxyfen, which is the major transformation product formed in water.

There is a potential for non-target terrestrial and aquatic habitats to be exposed to quinoxyfen as a result of spray drift or runoff. Quinoxyfen is not expected to pose a risk to terrestrial biota. Quinoxyfen may present a risk to aquatic organisms such as invertebrates, fish, plants, algae and amphibians. Additional information is being requested to further characterise the risk of quinoxyfen exposure to bees and beneficial arthropods, as well as the chronic risk of 2-oxo-quinoxyfen to aquatic organisms.

Value Considerations

What Is the Value of Quintec Fungicide?

Quintec Fungicide is being reviewed under the User Requested Minor Use Registration (URMUR) program to provide growers an effective tool for the control of powdery mildew on several fruits and vegetables. Quintec Fungicide has a novel and highly specific mode of action and will control powdery mildew biotypes that have become resistant to both demethylation-inhibitor (DMI) fungicides and potential strobilurin-resistance.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk-reduction measures being proposed on the label of Quintec Fungicide to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

Because there is a concern with users coming into direct contact with Quintec Fungicide on the skin, anyone mixing, loading and applying Quintec Fungicide must wear a long sleeved shirt, long pants, shoes plus socks and chemical resistant gloves. As an extra precaution, workers that handle the concentrated product are advised to wear coveralls, chemical resistant gloves, goggles and rubber boots. In addition, standard label statements to protect against drift during application were added to the label.

Environment

Quinoxyfen may present a risk to aquatic organisms such as invertebrates, fish, plants, algae and amphibians; therefore, additional advisory statements and buffer zones for aquatic habitats are required on the product label.

What Additional Scientific Information Is Being Requested?

Although the risks and value have been found acceptable when all risk-reduction measures are followed, the applicant must submit additional scientific information as a condition of registration. More details are presented in the Science Evaluation Section of this Evaluation Report or in the Section 12 Notice associated with these conditional registrations. The applicant must submit the following information.

Human Health

Information on the toxicity of 2-oxo-quinoxyfen, a major transformation product that accumulates in the environment, is required to characterize the potential risk to individuals exposed to 2-oxo-quinoxyfen through the drinking water.

Environment

The registrant is required to provide the following information:

For the parent compound quinoxyfen

- Acute oral toxicity study on bees
- Acute toxicity study on predators *(Typhlodromus pyri)*
- Acute toxicity study on parasites *(Aphidius rhopalosiphi)*

For the transformation product 2-oxo-quinoxyfen
Tier 1

- K_{ow} study
- Fish Early Life Cycle Toxicity Test

Based on the review of the results, additional information presented below could be required. Timelines to provide the data below would then be determined following the review of the above noted studies.

For the transformation product 2-oxo-quinoxyfen and/or quinoxyfen
Tier 2 (based on the study results to be provided at Tier 1)

- Fish Full Life Cycle Toxicity Test with 2-oxo-quinoxyfen
- Mesocosm study to address bioaccumulation and fate potential of quinoxyfen and 2-oxo-quinoxyfen

Other Information

As these conditional registrations relate to a decision on which the public must be consulted[3], the PMRA will publish a consultation document when there is a proposed decision on applications to convert the conditional registrations to full registrations or on applications to renew the conditional registrations, whichever occurs first.

The test data cited in this Evaluation Report (i.e. the test data relevant in supporting the registration decision) will be made available for public inspection when the decision is made to convert the conditional registrations to full registrations or to renew the conditional registrations (following public consultation). If more information is required, please contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (pmra.infoserv@hc-sc.gc.ca).

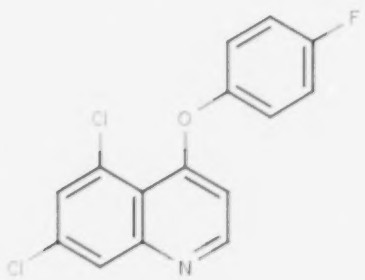
[3] As per subsection 28(1) of the *Pest Control Products Act*.

Science Evaluation

Quinoxyfen

1.0 The Active Ingredient, Its Properties and Uses

1.1 Identity of the Active Ingredient

Active substance	quinoxyfen
Function	fungicide
Chemical name	5,7-dichloro-4-(4-fluorophenoxy)quinoline
1. International Union of Pure and Applied Chemistry (IUPAC)	5,7-dichloro-4-quinolyl 4-fluorophenyl ether
2. Chemical Abstracts Service (CAS)	5,7-dichloro-4-(4-fluorophenoxy)quinoline
CAS number	124495-18-7
Molecular formula	$C_{15}H_8Cl_2FNO$
Molecular weight	308.1
Structural formula	
Purity of the active ingredient	92.10 %

1.2 Physical and Chemical Properties of the Active Ingredients and End-Use Product

Technical Product—Quinoxyfen Technical Fungicide

Property	Result
Colour and physical state	Off-white to beige, powdery solid
Odour	Odourless
Melting range	106.0 – 107.5°C
Boiling point or range	Not applicable to solid.

Density	1.49 g/mL at 20°C
Vapour pressure at 20°C	1.2×10^{-5} Pa
Ultraviolet (UV)-visible spectrum	Solution / λ_{max} (nm) / ε ($M^{-1}cm^{-1}$) Methanol / 297.3 / 9.49×10^3 Methanol / 236.8 / 6.49×10^4 Acidic / 317.4 / 9.57×10^3 Acidic / 242.8 / 5.05×10^4 Acidic / 210.6 / 2.73×10^4 Basic / 297.7 / 8.62×10^3 Basic / 236.9 / 6.30×10^4
Solubility in water at 20°C	0.116 mg/L (distilled water)
Solubility in organic solvents at 20°C	Solvent / Solubility (g/100mL) Hexane / 0.964 Dichloromethane / 58.9 Methanol / 2.15 Acetone / 11.6 Ethyl acetate / 17.9 Toluene / 27.2 n-Octanol / 3.79 Xylene / 20.0
n-Octanol-water partition coefficient (K_{OW})	pH / $\log K_{OW}$ 6.66 / 4.66
Dissociation constant (pK_a)	3.56
Stability (temperature, metal)	Stable to elevated temperatures and metals and metal ions.

End-Use Product—Quintec Fungicide

Property	Result
Colour	Off white
Odour	Faint earthy odour
Physical state	Liquid
Formulation type	Solution
Guarantee	Quinoxyfen at 250 g/L
Container material and description	Plastic bottle, jug or drum, 0.1 L to bulk
Density	1.097 g/mL at 20°C
pH of 1% dispersion in water	7.97
Oxidizing or reducing action	No significant oxidizing or reducing action
Storage stability	Stable for two years at ambient temperature and six months at 40°C in HDPE or PET containers.
Corrosion characteristics	Not corrosive to packaging materials.
Explodability	Not explosive from impact. Thermal explodability: exothermic event initiated at 290°C.

1.3 Directions for Use

Quintec Fungicide is a protectant fungicide for use on grapes, stone fruit, strawberry, hops, Lettuce, squash, pumpkin and melons. It is applied at the rate of 240–500 mL product/ha (60-125 g a.i./ha), with a maximum of five applications for grape, lettuce and stone fruit, four applications for melons, squash, pumpkin and strawberry and two applications for hops.

Quintec Fungicide will control or suppress the following pathogens that cause powdery mildew: *Uncinula necator* (on grape), *Sphaerotheca fuliginea* (on melons, swuash and pumpkin), *Erysiphe cichoraceearum* (on lettuce), *Podosphaera clandestina* and *Sphaerotheca pannosa* (on stone fruits) and *Sphaerotheca macularis* (on strawberry and hops).

1.4 Mode of Action

Quinoxyfen belongs to a novel class of fungicides called quinoline. Quinoxyfen disrupts fungi-specific cell-signaling events, which in turn interfere with the early stages of the powdery mildew disease life cycle (for example germination, early germ tube development, and /or appresoria formation). This mode of action differs from that of either of the two primary classes of synthetic, single-site fungicides (i.e. demethylation inhibitors and strobilurins) used to control powdery mildew.

Following foliar application, quinoxyfen peneterates into the leaf, binding preferentially to lipophilic surfaces such as the leaf cuticular waxes. Quinoxyfen is mobile within the plant cuticle, redistributing from the point of application to adjacent leaf, stem and fruit tissue through local movement.

2.0 Methods of Analysis

2.1 Methods for Analysis of the Active Ingredient

The methods provided for the analysis of the active ingredient and the impurities in Quinoxyfen Technical have been validated and assessed to be acceptable for the determinations.

2.2 Method for Formulation Analysis

The method provided for the analysis of the active ingredient in the formulation has been validated and assessed to be acceptable for use as an enforcement analytical method.

2.3 Methods for Residue Analysis

For environmental media, high-performance liquid chromatography methods with ultraviolet absorbance detection (HPLC/UV) and gas chromatography with either mass specific detection (GC-MSD) or tandem mass spectrometry (GC-MS/MS) were developed and proposed for data generation and enforcement purposes. These methods fulfilled the requirements with regards to selectivity, accuracy and precision at the respective method limit of quantification. Acceptable recoveries (70–120%) were obtained in environmental media. Methods for residue analysis are summarized in Appendix I, Table 1.

For plant commodities, a gas chromatography with mass-selective detection (GC-MSD) method was developed and proposed for data gathering and enforcement purposes. This method fulfilled the requirements with regards to specificity, accuracy and precision at the method limit of quantitation. Acceptable recoveries (70–120%) were obtained in plant matrices. The proposed enforcement method was successfully validated by an independent laboratory using hop samples as the most difficult matrix. Adequate extraction efficiencies were demonstrated using radiolabelled cucumber and grape samples analyzed with the enforcement method.

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

A detailed review of the toxicological database for quinoxyfen was conducted. The database is complete, consisting of the full array of toxicity studies currently required for hazard assessment purposes. The studies were carried out in accordance with currently accepted international testing protocols and Good Laboratory Practices. The scientific quality of the data is high and the database is considered adequate to define the majority of the toxic effects that may result from exposure to this chemical pest control product.

Quinoxyfen Technical Fungicide was of low toxicity by the oral, dermal and inhalation routes of exposure in rats. It was mildly irritating to the eyes and non-irritating to the skin of rabbits. Quinoxyfen was considered to be a dermal sensitizer according to the Maximization test method.

Quintec Fungicide was of low toxicity by the oral and dermal routes of exposure in rats. The waiver for the acute inhalation toxicity study was accepted and Quintec Fungicide was considered to be of low acute toxicity via the inhalation route. Quintec Fungicide was minimally irritating to the eyes and slightly irritating to the skin of rabbits. It was not a dermal sensitizer according to the Buehler test method.

In rats, quinoxyfen was rapidly absorbed, extensively metabolized and excreted primarily in the feces. Although quinoxyfen was fairly evenly distributed, it was found in greater levels in the fat, ovaries, liver, kidney, gastrointestinal tract and carcass. Quinoxyfen was extensively metabolized and the main metabolic pathway represented extensive cleavage of the diaryl-ether linkage of the parent compound resulting in formation of acid-labile conjugates of 4-fluorophenol (4-FP) and 5,7-dichloro-4-hydroxyguinoline (DCHQ) and lesser quantities of free DCHQ and 4-FP. The major metabolites found in bile were glucuronide and/or sulfate conjugates of two isomers of

fluorophenyl ring-hydroxy-quinoxyfen. No parent compound was found in the urine and only a trace amount was detected in the bile. Feces contained parent compound and unconjugated forms of the same two isomers of fluorophenyl ring-hydroxy-quinoxyfen were seen in the bile. There were no apparent differences in the metabolism and disposition of quinoxyfen between the sexes or single and repeated exposure.

5,7-dichloro-4-(4-flurophenoxy)-2-(1H)-quinolone, designated as "2-oxo-quinoxyfen", is a major accumulating environmental transformation product identified in the environmental fate studies and in the prospective groundwater monitoring studies. Based on the results of these studies, this transformation product is expected to reach groundwater when used in accordance with the label instructions. In a pharmacokinetics study, 2-oxo-quinoxyfen was only identified at very low levels (0.012% of the administered dose) in rat feces and therefore its toxicology profile has not been adequately addressed by the database for the parent compound and additional data are required.

No treatment-related systemic or dermal toxicity was observed up to a limit dose in rats after 28 days of dosing via the dermal route.

After repeated dietary dosing with quinoxyfen, the key treatment-related effects were decreased body weight/gains across the species tested, liver effects in mice and rats, and hemolytic regenerative anemia in dogs at higher doses. In the liver, the principal effects in rodents were increased organ weights associated with hepatocellular vacuolation, necrosis and/or hypertrophy. In a 90-day rat study, increased liver weights and hepatocellular hypertrophy at similar incidence and severity remained after a four-week recovery period. In rats and dogs, treatment-related small/atrophic testes and/or decreased spermatogenesis occurred at doses where liver toxicity was observed. There were no durational effects observed after quinoxyfen treatment. Rats were more sensitive to quinoxyfen-induced toxicity than mice or dogs.

In an 80-week mouse carcinogenicity study, there were no treatment-related effects other than decreased body weight gains in both sexes and decreased food efficiency in females. No evidence of carcinogenicity was observed. In a two-year combined chronic/carcinogenicity study in rats, decreased body weight gains and food consumption were observed in both sexes and chronic progressive nephropathy was observed in males. The key treatment-related renal effects included moderate chronic progressive glomerulonephropathy, increased blood urea nitrogen and a roughened kidney surface. There was no evidence of carcinogenic potential.

In a two-generation reproductive toxicity study, no adverse effects were observed in the parental animals. Treatment-related decreases in pup body weight (males and females) and overall body weight gains were observed in the high dose F_{1a}, F_{1b} and F_2 litters during lactation. Post-weaning pup body weights in the treated groups were comparable to controls. Starting at approximately postnatal day 17, rat pups often begin to consume feed and due to simultaneous exposure to the compound via maternal milk and dietary consumption, pups may have an increased compound intake per unit body weight relative to the adults. The result is a probable enhancement of toxicity based on a higher systemic dose rather than an age-related sensitivity. Although this may explain the body weight decrements observed during the latter part of lactation, the body weight effect observed earlier in the preweaning period (lactation days 1–14) likely occurred prior to

consumption of treated diet by the pups. Although treatment-related, these effects were marginal and of a magnitude that was similar to that of adult body weight effects in other toxicity studies at comparable dose levels. Therefore, the pup body weight effects observed at maternally non-toxic doses were considered to be of low toxicological concern.

In a rat developmental toxicity study, no maternal or developmental toxicity was observed up to a limit dose. In a rabbit developmental toxicity study, maternal toxicity was observed as decreased body weight gains and food consumption, clinical signs (decreased fecal output, soft feces, perineal soiling, blood or urine contained blood in the cage pan) and increased incidences of late gestation abortions at high doses. There was no evidence of teratogenicity in rabbits.

No evidence of mutagenic potential for quinoxyfen was observed in a battery of in vitro and in vivo genotoxicity assays assessing gene mutation and chromosome aberration.

Quinoxyfen was not neurotoxic as demonstrated in acute and 1-year neurotoxicity studies in rats. The only treatment-related effect in the 1-year neurotoxicity study was a marginal decrease in body weight gain in females. There were no triggers in the toxicological database to warrant a study to investigate developmental neurotoxicity.

Results of the acute and chronic tests conducted on laboratory animals with quinoxyfen technical and its associated end-use product, along with the toxicology endpoints for use in the human health risk assessment, are summarized in Appendix I, Tables 2, 3 and 4.

In assessing the occupational and dietary risks from potential exposure to quinoxyfen products, the standard uncertainty factor of 100 has been applied to account for interspecies extrapolation and intraspecies variability.

3.1.1 PCPA Hazard Characterization

For assessing risks from potential residues in food or from products used in or around homes or schools, the *Pest Control Products Act* requires the application of an additional 10-fold factor to take into account completeness of the data with respect to the exposure of, and toxicity to, infants and children and potential prenatal and postnatal toxicity. A different factor may be determined to be appropriate on the basis of reliable scientific data.

With respect to the completeness of the toxicity database, extensive data were available for quinoxyfen including developmental toxicity studies in rats and rabbits and a two-generation rat reproductive toxicity study.

With respect to effects relevant to the assessment of risk to infants and children, no evidence of increased susceptibility was seen following in utero exposure to rats or rabbits in the developmental toxicity studies. The abortions seen in the rabbit in a developmental toxicity study occurred late in gestation and were associated with maternal toxicity at high doses. Although the observed effect was considered a serious endpoint, the concern was tempered by the presence of maternal toxicity. When the no observed adverse effect level (NOAEL) for developmental effects are compared with the NOAEL used for human risk assessment, a margin of 10-fold is

provided. In the rat reproductive toxicity study, decreased body weights and body weight gains were observed in offspring during lactation. Although the observed effect occurred at maternally non-toxic doses, the concern was offset by the marginal magnitude and nature of the effect, the absence of offspring body weight effects post-weaning and the presence of similar body weight effects in adults at comparable dose levels in other studies. Consequently, there was a low level of concern for pre or postnatal toxicity associated with quinoxyfen. Given the low level of concern for pre and postnatal toxicity and the completeness of the database, the PCPA factor was reduced from 10-fold to 1-fold.

3.2 Determination of Acute Reference Dose

An acute reference dose for quinoxyfen was not determined for the general population (including females aged 13–49, infants and children) because an endpoint of concern attributable to a single exposure was not identified in the oral toxicity studies.

3.3 Determination of Acceptable Daily Intake

The recommended acceptable daily intake (ADI) for quinoxyfen is based on a NOAEL of 20 mg/kg bw/day from the two-year combined chronic/carcinogenicity study in rats. This was supported by the NOAELs of 20 mg/kg bw/day in the 12-month dog study and the rat reproductive toxicity study. In the selected chronic study, treatment-related decreases in body weights and histopathological liver alterations (hypertrophy, slight necrosis and increased size of hepatocytes) occurred at the lowest observed adverse effect level (LOAEL) of 80 mg/kg bw/day. Uncertainty factors of 10-fold for interspecies extrapolation as well as a 10-fold for intraspecies variability were applied in the setting of the ADI. As indicated above in the PCPA Hazard Characterization section, the PCPA factor was reduced to 1-fold, resulting in a composite assessment factor (CAF) of 100-fold.

The ADI is calculated according to the following formula:

$$\text{ADI} = \frac{\text{NOAEL}}{\text{CAF}} = \frac{20 \text{ mg/kg bw/day}}{100} = 0.2 \text{ mg/kg bw/day of quinoxyfen}$$

3.4 Occupational and Residential Risk Assessment

3.4.1 Toxicological Endpoints

Occupational exposure to Quintec Fungicide is characterized as short- to intermediate-term and is predominantly by the dermal and inhalation routes.

Short-term to intermediate-term dermal

A rat 21-day dermal toxicity study was available for quinoxyfen and was considered to be the most appropriate endpoint for dermal risk assessment. The NOAEL in this study was 1000 mg/kg bw/day, the highest dose tested. Use of this endpoint is considered protective of all sub-populations, including nursing infants and unborn children of exposed female workers. The

standard uncertainty factors (10-fold for interspecies extrapolation and 10-fold for intraspecies variability) applied provide a target margin of exposure (MOE) of 100.

Short-term to intermediate-term inhalation

No repeat-dose inhalation toxicity studies were available for quinoxyfen. The offspring NOAEL of 20 mg/kg bw/day from the oral reproductive toxicity study represented the highest NOAEL for the endpoint of concern (decreased body weights) and was considered to be the most appropriate endpoint for inhalation risk assessment. The selected endpoint was based on decreased body weights and body weight gains during lactation in F_1 and F_2 pups at the LOAEL of 100 mg/kg bw/day. The target MOE is 100 for the reasons outlined above in the dermal endpoint selection section. The selection of this study and this MOE is considered to be protective of all populations, including nursing infants and unborn children of exposed female workers.

3.4.2 Occupational Exposure and Risk

3.4.2.1 Mixer/Loader/Applicator Exposure and Risk Assessment

Individuals have potential for exposure to Quintec Fungicide during mixing, loading and application. Dermal and inhalation exposure estimates for workers mixing, loading and applying were generated from the Pesticide Handlers Exposure Database (PHED) since chemical-specific data for assessing human exposures during pesticide handling activities was not submitted.

Exposure to workers mixing, loading and applying Quintec Fungicide is expected to be short- to intermediate-term in duration and to occur primarily by the dermal and inhalation routes. Exposure estimates were derived for mixer/loaders/applicators applying Quintec Fungicide to stone fruit, hops, and grapes using airblast equipment and to strawberries, melons, pumpkins, winter squash, head and leaf lettuce and hops using groundboom equipment. The exposure estimates are based on mixers/loaders/applicators wearing long sleeves, long pants and chemical-resistant gloves.

Dermal exposure was estimated by coupling the unit exposure values with the amount of product handled per day. A dermal absorption value was not required since the dermal endpoint is based on a dermal toxicology study. Inhalation exposure was estimated by coupling the unit exposure values with the amount of product handled per day with 1000sd% inhalation absorption. Exposure was normalized to mg/kg bw/day by using 70 kg adult body weight.

Exposure estimates were compared to the toxicological endpoints (NOAELs) to obtain the MOE; the target MOE is 100. All MOEs are above the target for mixer, loaders and applicators wearing long-sleeves, long pants and chemical-resistant gloves (Table 3.4.1).

Table 3.4.1: Mixer/Loader/Applicator Dermal Exposure Estimates and Margins of Exposure (MOEs)

Crop	Rate (kg a.i./ha)	Area Treated per Day (ha)	Dermal Exp. Estimates [a] (mg/kg bw/day)	Inhalation Exp. Estimate [a] (mg/kg bw/day)	Dermal MOE[b]	Inhalation MOE[c]
Melons, pumpkins, winter squash	0.11	26	0.0034	0.0001	291 000	191 000
Grapes	0.075	20	0.0131	0.0002	76 100	126 000
Hops (farmer-airblast)	0.125	20	0.0219	0.0003	45 700	75 700
Hops (farmer - groundboom)	0.125	26	0.0039	0.0001	256 000	168 000
Hops (custom – groundboom applicator)	0.125	360	0.0541	0.0016	18 500	12 200
Head and Leaf Lettuce	0.06	20	0.0014	0.00001	693 000	456 000
Strawberries	0.11	20	0.0026	0.0001	378 000	249 000
Stone fruit	0.125	20	0.0219	0.0003	45 700	75 700

[a] Exposure Estimates= $\frac{\text{PHED Exposure (µg a.i./kg a.i. handled) x Rate (kg a.i. handled) x Area Treated per Day (ha)}}{\text{body weight (kg) x 1000 µg/mg}}$

[b] Dermal MOE = 1000 mg/kg bw/day/ Dermal Exposure (mg/kg bw/day); target MOE = 100

[c] Inhalation MOE = 20 mg/kg bw/day/ Inhalation Exposure (mg/kg bw/day); target MOE = 100

3.4.2.2 Exposure and Risk Assessment for Workers Entering Treated Areas

There is potential for workers entering treated fields to perform routine re-entry activities to be exposed to residues of quinoxyfen on foliage. Exposure is expected to be of short- to intermediate-term in duration and to occur primarily by the dermal route. Since no chemical specific dislodgeable foliar residue (DFR) data was submitted, a default DFR value of 20% of the application rate on the day of application with a 10% daily dissipation rate was used to estimate risk to workers contacting treated foliage. Up to five applications may be made to grapes and stone fruit, up to four on strawberries, melons, pumpkins, winter squash and lettuce and two on hops. It was assumed that these applications are made at the minimum treatment interval (10 or 14 days depending on crop). For each crop, the DFR value on the day of the last application using the highest approved rate was used to estimate postapplication exposure. A dermal absorption value was not required since the dermal endpoint is based on a dermal toxicology study. Postapplication exposure was calculated using the following equation:

$$\text{Exposure} = \frac{\text{DFR}(\mu g/cm^2) \times \text{Transfer Coefficient } (cm^2/h) \times \text{Exposure Duration (8 hours)}}{\text{Body Weight (kg)} \times 1000\ \mu g/mg} \text{ (mg/kg bw/day)}$$

As a tier one approach, the highest transfer coefficient for each crop was used to estimate postapplication exposure for each crop group (Table 3.4.2). Dermal MOEs were calculated based on a NOAEL of 1000 mg/kg bw/day. The target MOE is 100. MOEs are above the target of 100 on the day of the final application.

Table 3.4.2 Postapplication Margin of Exposures (MOEs) to Quintec Fungicide

Crop	Activity	Exposure (mg/kg bw/day)[a]	MOE[b]
Melons, pumpkins, winter squash	Hand-harvesting, leaf pulling, hand pruning, thinning, turning	0.0951	10 500
Grapes	Girdling, cane turning	0.4288	2 330
Hops	Hand harvesting, mechanical harvesting, stripping, training	0.0702	14 200
Head and Leaf Lettuce	Hand-harvesting, hand pruning, thinning	0.0519	19 300
Strawberries	Hand-harvesting, thinning, hand pruning, tying	0.0571	17 500
Stone fruit	Thinning	0.1309	7 640

a Estimated as Dislogeable residue on the day of the last application (µg/cm^2) × transfer coefficient (cm^2 /hour) × 8 hour/day worked / 70 kg body weight

b NOAEL/ Exposure; target MOE = 100.

3.4.3 Residential Exposure and Risk Assessment

Since there are no residential uses for Quintec Fungicide, a residential risk assessment was not required.

3.4.3.1 Bystander Exposure and Risk

Bystander exposure should be negligible since the potential for drift is expected to be minimal. Application is limited to agricultural crops only when there is low risk of drift to areas of human habitation or activity such as houses, cottages, schools and recreational areas, taking into consideration wind speed, wind direction, temperature inversions, application equipment and sprayer settings.

3.5 Food Residues Exposure Assessment

3.5.1 Residues in Plant and Animal Foodstuffs

The residue definition for risk assessment and enforcement in plant products is quinoxyfen. The GC-MSD enforcement analytical method is valid for the quantification of quinoxyfen residues in plant matrices. The residues of quinoxyfen are stable when stored in a freezer at -18°C for six months in apple, apricot, peach, strawberry, artichoke and zucchini, and 12 months in grapes. Raw agricultural commodities were processed, and quinoxyfen residues only concentrated in the processed commodity of dried prune plums (3.5x). There are no livestock or poultry feed items associated with the crops in the current use pattern, therefore quantifiable residues are not expected to occur in livestock matrices. Supervised residue trials conducted throughout the United States and Canada using end-use products containing quinoxyfen at approved or exaggerated rates in or on cantaloupes, cherries, grapes, hops, lettuce, peaches, plums, strawberries and winter squash are sufficient to support the proposed maximum residue limits.

3.5.2 Concentrations in Drinking Water

Estimated environmental concentrations (EECs) of combined residues (quinoxyfen plus transformation product 2-oxo-quinoxyfen[4]) in potential drinking water sources (groundwater and surface water) were estimated using computer simulation models. An overview of how the EECs are estimated is provided in the PMRA's Science Policy Notice SPN2004-01, *Estimating the Water Component of a Dietary Exposure Assessment*. EECs of combined residues in groundwater were calculated using the LEACHM model to simulate leaching through a layered soil profile over a 50-year period. The concentrations calculated using LEACHM are based on the flux, or movement, of pesticide into shallow groundwater with time. EECs of combined residues in surface water were calculated using the PRZM/EXAMS models, which simulate pesticide runoff from a treated field into an adjacent water body and the fate of a pesticide within that water body. Pesticide concentrations in surface water were estimated in two types of vulnerable drinking water sources, a small reservoir and a prairie dugout.

In the current assessment, a combined residue of the parent and the transformation product 2-oxo-quinoxyfen was modelled for drinking water. Thus, environmental half-lives in soil and water were calculated for the combined residues of parent and 2-oxo-quinoxyfen.

A Level 1 drinking water assessment was conducted using conservative assumptions with respect to environmental fate, application rate and timing, and geographic scenario. The model inputs are reported in Appendix I, Table 8. The Level 1 EEC estimate is expected to allow for future use expansion into other crops at this application rate. Eight initial application dates between May and June were modelled. The models were run for 50 years for all scenarios. The largest EECs of all selected runs are reported in Appendix I, Table 9.

Details of water modelling inputs and calculations are available upon request.

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[4] Up until 2005, one major transformation product of quinoxyfen had been identified as 3-OH-quinoxyfen. Since then, it has been confirmed to be 2-oxo-quinoxyfen.

3.5.3 Dietary Risk Assessment

Chronic dietary risk assessments were conducted using the Dietary Exposure Evaluation Model (DEEM–FCID™, Version 2.16), which uses updated food consumption data from the United States Department of Agriculture's Continuing Surveys of Food Intakes by Individuals, 1994–1996 and 1998.

3.5.3.1 Chronic Dietary Exposure Results and Characterization

For the basic chronic analysis, Maximum Residue Limits (MRLs) for all crops were used. The basic chronic dietary exposure from all supported quinoxyfen food uses for the total population is 1.3% of the ADI. Aggregate exposure from food and water is considered acceptable. The PMRA estimates that chronic dietary exposure to quinoxyfen from food and water is 1.3% of the ADI (0.002572 mg/kg bw/day) for the total population. The highest exposure and risk estimate is for children one to two years old at 2.1% of the ADI (0.004190 mg/kg bw/day).

3.5.3.2 Acute Dietary Exposure Results and Characterization

No appropriate endpoint attributable to a single dose for the general population (including children and infants) was identified. Therefore, no acute dietary exposure assessment was conducted.

3.5.4 Aggregate Exposure and Risk

The aggregate risk for quinoxyfen consists of exposure from food and drinking water sources only; there are no residential uses. Aggregate risks were calculated based on chronic endpoints. There was no acute endpoint identified for the general population, including infants and children.

3.5.5 Maximum Residue Limits

Table 3.5.1 Proposed Maximum Residue Limits

Commodity	Recommended MRL (ppm)
Leaf lettuce	19.0
Head lettuce	7.0
Strawberries	0.9
Crop Group 12-09 (Stone Fruits Group)	0.7
Pumpkins	0.2
Winter squash	0.2
Crop Subgroup 9A (Cucurbit Vegetable Group - Melon Subgroup)	0.08

For additional information on MRLs in terms of the international situation and trade implications, refer to Appendix II.

The nature of the residues in animal and plant matrices, analytical methodology, field trial data, and the chronic dietary risk estimates are summarized in Appendix I, Tables 1, 5 and 6.

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

Based on its physico-chemical properties, quinoxyfen is sparingly soluble in water, with solubility tending to decrease with rising pH. It is not likely to volatilise from moist soil under field conditions but could be slightly volatile from a water surface. Since quinoxyfen is classified as having low volatility, volatilisation into the air is not expected to be a main route of dissipation. Quinoxyfen is not expected to undergo long range transport due to its low vapour pressure. Quinoxyfen is expected to have a limited potential for direct phototransformation under natural light conditions. The log K_{ow} indicates that quinoxyfen could potentially bioaccumulate in aquatic organisms.

Data on the environment fate and behaviour of quinoxyfen and its transformation products are summarized in Appendix I, Tables 7 to 10.

Quinoxyfen enters the soil when used as a fungicide for various crops. Laboratory studies indicate that hydrolysis and phototransformation in soil are not expected to be an important route of transformation for quinoxyfen. Based on a laboratory study, it is expected that biotransformation in aerobic soil will vary with temperature and quinoxyfen can be moderately persistent under warmer conditions (30°C) to persistent under colder (15 and 25°C) conditions. Quinoxyfen is expected to slowly transform into 2-oxo-quinoxyfen, DCHQ and other minor products. Although half-lives could not be calculated, this study indicates that 2-oxo-quinoxyfen may be persistent, because this transformation product reached a maximum level of 67.5% of the applied parent concentration by the end of the experiment with no sign of decline. In anaerobic soil, a biotransformation study has shown that quinoxyfen was persistent; it either was slowly bound to soil or was transformed to the major transformation product 2-oxo-quinoxyfen. At the end of the study (100 days), quinoxyfen was present at 72%, 2-oxo-quinoxyfen at 6% and 19% of the residues were bound to soil and could not be extracted. Laboratory studies indicate that quinoxyfen is expected to be immobile and have a low potential to leach under normal use conditions, 2-oxo-quinoxyfen would be immobile in any soil and DCHQ would be of low mobility to immobile. Therefore, 2-oxo-quinoxyfen is not expected to leach. A simulation model used to simulate leaching of the combined residues of quinoxyfen and 2-oxo-quinoxyfen through a layered soil profile over a 50-year period indicated that no residues are expected in groundwater. In the field study conducted in Canada, both 2-oxo-quinoxyfen and DCHQ tended to stay in the upper soil layer. A terrestrial field study conducted in Canada has shown results consistent with laboratory studies conducted at 30°C, as quinoxyfen was moderately persistent (DT_{50} = 83.6 days). 2-oxo-quinoxyfen and DCHQ showed maximum concentrations of 3.7% and 7.7% of the applied amount at 392 and 62 days, respectively. Half-lives for the transformation products could not be adequately calculated. In this study, a carryover of 15% of the applied amount of quinoxyfen on soil was observed at the beginning of the next growing season. Field studies from Europe have shown higher percentages. Laboratory studies on soil have indicated a

significant impact of temperature on the rate of degradation of quinoxyfen, which could explain these discrepancies.

Quinoxyfen can enter the aquatic environment through spray drift and runoff. Once in the water, quinoxyfen is not expected to hydrolyse. Phototransformation is expected to be an important route of transformation of quinoxyfen when the compound is present under acidic conditions in the photic zone (top six inches) of clear surface water. The resulting major transformation product, CFBBQ, also phototransforms rapidly into two unidentified major transformation products, which reach maximum concentrations within a day. After seven days, quinoxyfen and all three major transformation products were below the limit of quantification (LOQ). Numerous minor transformation products were isolated in this study. Based on a laboratory biotransformation study in water and sediment, quinoxyfen is expected to rapidly partition to the sediment where it will biotransform. Half-life values for a water-sediment system indicated that quinoxyfen was slightly persistent. 2-oxo-quinoxyfen was the resulting major transformation product, mostly present in the sediment, where it reached a maximum concentration at 48 days. A half-life could not be estimated since the only other available data were at the end of the 100-day study. At the end, quinoxyfen, 2-oxo-quinoxyfen and unextractable residues accounted for 24, 33 and 21% of the initial applied amount of radioactivity, respectively. Quinoxyfen was non-persistent under anaerobic conditions in the watersediment anaerobic biotransformation study. 2-oxo-quinoxyfen was the major transformation product, which continued to increase until study termination, indicating it may be persistent in sediment. In water, DCHQ is a minor transformation product and was only formed under aerobic conditions.

Based on its physico-chemical properties, quinoxyfen is not expected to be susceptible to long range transport. An atmospheric half-life of 1.88 days was also estimated, using the Atmospheric Oxidation Program from the Syracuse Research Corporation. This value is just below the TSMP criteria for persistence in air (see Section 6). A preliminary review of a monitoring study on quinoxyfen deposition in Sweden indicated a low potential for long range transport. At this time, there is no indication of concerns about the persistence of quinoxyfen in air and its potential for long range transport.

Quinoxyfen has the potential to bioaccumulate, as indicated by its log K_{ow} of 4.66 and a bioconcentration factor of 5040 in a fish study. However, in this study, the fish showed rapid depuration when placed in clean water. In a rat metabolism study, there was no evidence of bioaccumulation; quinoxyfen was rapidly absorbed, extensively metabolized and almost fully excreted.

In the field, a preliminary review of biota monitoring studies from Europe indicated some bioaccumulation in earthworms. Residues were also quantified in aquatic macroinvertebrates and some fish species. Estimated bioaccumulation factors (BAFs) up to 13 were calculated for earthworms, but accurate bioaccumulation factors could not be calculated for aquatic biota given the lack of data on water concentrations and non-detected concentrations in sediment. Based on the low levels of quinoxyfen concentrations in organisms, no substantial bioaccumulation would be expected.

4.2 Environmental Risk Characterization

The environmental risk assessment integrates the environmental exposure and ecotoxicology information to estimate the potential for adverse effects on non-target species. This integration is achieved by comparing exposure concentrations with concentrations at which adverse effects occur. Estimated exposure concentrations (EECs) are concentrations of pesticide in various environmental media, such as food, water, soil and air. The EECs are estimated using standard models which take into consideration the application rate(s), chemical properties and environmental fate properties, including the dissipation of the pesticide between applications. Ecotoxicology information includes acute and chronic toxicity data for various organisms or groups of organisms from both terrestrial and aquatic habitats including invertebrates, vertebrates, and plants. Toxicity endpoints used in risk assessments may be adjusted to account for potential differences in species sensitivity as well as varying protection goals (i.e. protection at the community, population, or individual level).

Initially, a screening level risk assessment is performed to identify pesticides and/or specific uses that do not pose a risk to non-target organisms, and to identify those groups of organisms for which there may be a potential risk. The screening level risk assessment uses simple methods, conservative exposure scenarios (for example, direct application at a maximum cumulative application rate) and sensitive toxicity endpoints. A risk quotient (RQ) is calculated by dividing the exposure estimate by an appropriate toxicity value (RQ = exposure/toxicity), and the risk quotient is then compared to the level of concern (LOC).

If the screening level risk quotient is below the level of concern, the risk is considered negligible and no further risk characterization is necessary. If the screening level risk quotient is equal to or greater than the level of concern, then a refined risk assessment is performed to further characterize the risk. A refined assessment takes into consideration more realistic exposure scenarios (such as drift to non-target habitats) and might consider different toxicity endpoints. Refinements may include further characterization of risk based on exposure modelling, monitoring data, results from field or mesocosm studies, and probabilistic risk assessment methods. Refinements to the risk assessment may continue until the risk is adequately characterized or no further refinements are possible.

4.2.1 Risks to Terrestrial Organisms

A risk assessment of quinoxyfen to terrestrial organisms was based on an evaluation of quinoxyfen toxicity data for earthworms (acute contact), bees (acute contact), two species of birds (acute oral, dietary, and chronic), mammals (acute oral and chronic), and terrestrial plants (seedling emergence and vegetative vigour). A summary of toxicity data for quinoxyfen is presented in Appendix I, Table 11. For the risk assessment, the toxicity endpoints chosen from the most sensitive species were used as surrogates for the wide range of species that can be potentially exposed following treatment with quinoxyfen (Appendix I, Table 12). The screening level risk assessment was determined based on the EECs for the highest use rate scenario for quinoxyfen (625 g a.i./ha).

Earthworms: Quinoxyfen is practically non-toxic to earthworms on an acute basis (greater than 619 mg a.i./kg soil).The screening LOC was not exceeded (Appendix I, Table 13).

Bees (pollinators): Quinoxyfen is practically non-toxic to bees when exposed by contact on an acute basis. The screening LOC was not exceeded (Appendix I, Table 13). Additional data are required to address the acute risk to bees from ingesting quinoxyfen residues.

Beneficial arthropods: Data are required to address the risk to beneficial arthropods.

Birds: Quinoxyfen was not toxic to bobwhite quail (*Colinus virginianus*) on an acute oral basis, with no treatment-related mortalities occurring. During short-term dietary exposure to bobwhite quail and mallard duck, no treatment-related mortality occurred. However, both species experienced a reduction in weight gain. Reduction of weight was observed at the two highest concentrations tested for mallard duck. During reproduction studies on bobwhite quail and mallard duck, respectively, no treatment-related effects were observed for adult mortality, body weight or food consumption. Overall reproductive success was not adversely affected in bobwhite quail, but was reduced in mallard duck, in the highest treatment group. The risk quotients for acute and reproductive exposure to birds at the screening level risk assessment do not exceed the LOC for small, medium or large birds (Appendix I, Tables 14 and 15).

Mammals: The laboratory toxicity of quinoxyfen to rats was used to assess risk to small terrestrial mammals. Quinoxyfen, 53.9% and 41.3% end-use product formulations were not acutely toxic to rats (Appendix I, Table 11). In the rat reproduction study, reduced body weight and body weight gain in offspring were observed, however, they were of marginal toxicological significance and the overall reproductive performance in rat was not considered affected by exposure to quinoxyfen. The risk quotients for acute exposure to mammals at the screening level risk assessment do not exceed the LOC for small, medium or large mammals (Appendix I, Tables 14 and 15). A slight risk to reproduction for medium size mammals was identified (RQ = 1.1). However, considering the risk quotient is just above the threshold of one for the level of concern (1.1) and the conservative exposure and toxicity scenarios of the screening level assessment, no further characterization of the risk was deemed necessary. The use of quinoxyfen is not expected to pose an unacceptable reproductive risk to mammals at an application rate of 625 g a.i./ha.

Non-target plants: The toxicity of a 251 g/L formulated product of quinoxyfen to non-target plants was determined through vegetative vigour and seedling emergence assays using standard crop species. No significant adverse effects (i.e., >25% effect) were observed in any plant species in the seedling emergence assay. In the vegetative vigor assay, a dose-response pattern was observed in cucumber as fresh weight decreased with increasing concentrations (6.5–29.3%). Therefore, the EC_{25} for seedling emergence and vegetative vigor are >553 and 410 g a.i./ha, respectively (Appendix I, Table 11). The screening level risk assessment for the most sensitive end-point determined that the LOC was not exceeded. Therefore, quinoxyfen is not expected to impact non-target terrestrial plants adjacent to the treatment area.

4.2.2 Risks to Aquatic Organisms

Aquatic organisms can be exposed to quinoxyfen as a result of spray drift and over-land run-off. To assess the potential for adverse effects, screening level EECs in the aquatic environment based on a direct application to water following application of quinoxyfen to stone fruit and strawberry were used as the exposure estimates. A risk assessment of quinoxyfen, a 250 g/L formulation, was undertaken for freshwater and marine organisms based upon the evaluation of toxicity data for invertebrates, fish, vascular plants and algae in freshwater, and invertebrates, fish and diatoms in estuarine/marine environments.

It should be noted that some fate and physico-chemical properties of quinoxyfen can present challenges for studies conducted in water, where quinoxyfen concentrations need to be maintained for a given period. These constitute additional uncertainties related to the actual exposure of aquatic organisms to quinoxyfen, which could influence endpoint values used in the risk assessment. As an example, quinoxyfen is sparingly soluble in distilled water at 20°C (0.116 mg/L) and its solubility tends to decrease with rising pH. Quinoxyfen will also strongly sorb to glass and will partition quickly to sediment. In addition, the phototransformation of quinoxyfen in water is very rapid, which needs to be considered in aquatic studies conducted under light conditions. Certain solvents used to increase quinoxyfen solubility might also act as photosensitizers that could increase the phototransformation rate of quinoxyfen. Therefore, it is expected that quinoxyfen concentrations may not remain constant following initial dosing, and where possible, mean measured concentrations were used to characterize quinoxyfen exposure.

A summary of toxicity data for quinoxyfen and two major transformation products is presented in Appendix I, Table 11. For the risk assessment, the toxicity endpoints chosen from the most sensitive species were used as surrogates for the wide range of species that can be potentially exposed following treatment with quinoxyfen. Risk to amphibians was assessed based on surrogate data for freshwater fish (Appendix I, Table 12).

Freshwater invertebrates: In laboratory studies, quinoxyfen was acutely toxic to the aquatic invertebrate *Daphnia magna*. Acute toxicity of the major transformation products 2-oxo-quinoxyfen and DCHQ were also tested on *Daphnia magna*. For both transformation products, no toxic effects were noted up to the highest concentrations tested. A chronic exposure of *Daphnia magna* to quinoxyfen had negative effects on mean length and reproduction. A chronic exposure of the freshwater midge *Chironomus riparius* to quinoxyfen had negative effects on growth and maturity rate. A chronic exposure of 2-oxo-quinoxyfen had no effect on the emergence and development rate of *Chironomus riparius* (Appendix I, Table 11).

Screening level risk quotient values for acute or chronic quinoxyfen exposure were greater than the level of concern, indicating that further refinement was necessary (Appendix I, Table 16). Risk quotient values were also calculated for the transformation products 2-oxo-quinoxyfen and DCHQ, assuming 100% transformation from quinoxyfen. For DCHQ, the RQ from acute exposure was below the LOC. For 2-oxo-quinoxyfen, the RQs from acute exposure to *Daphnia magna* and chronic exposure to chironomid were below the LOC (Appendix I, Table 16).

The refined risk quotients based on spray drift of quinoxyfen slightly exceed the LOC for chronic exposure of the freshwater invertebrate *Daphnia magna* from airblast applications (Appendix I, Table 17). Therefore, there is a potential risk to freshwater invertebrates exposed to quinoxyfen through spray drift from airblast application.

Refined risk quotients based on runoff inputs did not exceed the LOC for freshwater invertebrate species, indicating that these organisms are not expected to be at risk from quinoxyfen runoff into water bodies (Appendix I, Table 18).

Freshwater fish and amphibians: In laboratory studies, quinoxyfen was acutely toxic to rainbow trout and carp. It was not acutely toxic to bluegill sunfish up to the highest measured concentration tested. Acute toxicity of the major transformation product 2-oxo-quinoxyfen was also tested on rainbow trout and no toxic effects were noted up to the highest concentration tested. Mortality and sublethal effects were also observed from chronic exposure of rainbow trout to quinoxyfen. The most sensitive endpoint of all freshwater species was from an early life stage toxicity test with quinoxyfen on fathead minnow, where juvenile fish length was affected. Juvenile fish survival was also significantly affected at 0.112 mg/L. (Appendix I, Table 11). Screening level risk quotient values for acute or chronic quinoxyfen exposure were greater than the level of concern, indicating that further refinement was necessary (Appendix I, Table 16). A risk quotient was also calculated for the transformation product 2-oxo-quinoxyfen, assuming 100% transformation from quinoxyfen. The RQ from an acute exposure to rainbow trout was less than a value above the LOC, due to the lack of toxicity at the highest concentration tested. Therefore, a refined risk assessment was conducted to determine the risk associated with drift and runoff. The refined risk quotients based on spray drift of quinoxyfen slightly exceed the LOC for chronic exposure of the fathead minnow and the rainbow trout from airblast applications to stone fruits (Appendix I, Table 17). Therefore, there is a potential risk to freshwater fish exposed to quinoxyfen through spray drift from airblast application. Refined risk quotients based on runoff inputs did not exceed the LOC for freshwater fish species, indicating that these organisms are not expected to be at risk from quinoxyfen runoff into water bodies (Appendix I, Table 18).

The risk for amphibians was characterized at the screening level by comparing EECs in 15 cm of water with fish toxicity endpoints as surrogates for aquatic life-stages of amphibians. Acute risks were assessed for exposure to quinoxyfen and the transformation product 2-oxo-quinoxyfen, as well as chronic risk was assessed for quinoxyfen. The screening level risk quotients for amphibians exceeded the LOC (Appendix I, Table 16). Refined risk quotients based on spray drift of quinoxyfen exceeded the LOC for acute and early life stage exposures from airblast applications and from groundboom applications (Appendix I, Table 17), indicating a potential risk. Refined risk quotients based on runoff inputs slightly exceeded the LOC for amphibians, indicating that these organisms could be at risk from quinoxyfen runoff into water bodies (Appendix I, Table 18). However, the most conservative EEC value of the ecoscenario (peak of 18 µg a.i./L) was used; using the second highest EEC from modelling with the surrogate endpoint used for amphibians, an estimated concentration of 2.2 µg a.i./L at 96 hours, the RQ is reduced to 0.2, below the level of concern. Therefore, these organisms are not expected to be at risk from quinoxyfen runoff into water bodies.

Freshwater algae and plants: Three algal and one plant species were tested for toxicity in laboratory studies. Quinoxyfen was toxic to green algae (*Selenastrum capricornutum*), diatom (*Navicula pelliculosa*) and duck weed (*Lemna gibba*). Quinoxyfen was not toxic to blue-green alga *Anabaena flos-aquae* up to the highest concentration tested. The transformation product DCHQ was tested on green algae and was not toxic up to the highest concentration tested (Appendix I, Table 11). The screening level risk quotient for green algae and diatom exposed to quinoxyfen exceeded the LOC (RQs > 1; Appendix I, Table 16). Refined risk quotients based on spray drift of quinoxyfen slightly exceeded the LOC for airblast application; the LOC was not exceeded for field sprayer application (Appendix I, Table 17). Therefore, there is a potential risk to freshwater algae from some airblast application uses. Algae are not expected to be at risk from quinoxyfen runoff inputs (Appendix I, Table 18). Screening level risk quotient for green algae exposed to the transformation product DCHQ did not exceed the LOC.

For the freshwater plant, duckweed, the screening level risk quotient for exposure to quinoxyfen for all uses did not exceed the LOC (Appendix I, Table 16).

Marine/estuarine species: In laboratory studies, quinoxyfen was acutely toxic to the saltwater diatom (*Skeletonema costatum*), Eastern oyster (*Crassostrea virginica*) and mysid shrimp (*Americamysis bahia*). It was not acutely toxic to the sheepshead minnow (*Cyprinodon variegatus)* up to the highest concentration tested. However, in the chronic study, exposure to quinoxyfen for 39 days resulted in reduced reproduction of sheepshead minnow, while exposure to quinoxyfen to early life stages of sheepshead minnow affected fry survival (Appendix I, Table 11). The screening level risk quotients based on acute, chronic and/or early life stage exposures of marine/estuarine invertebrates, fish and algae exceeded the LOC (Appendix I, Table 16). Refined risk quotients based on spray drift of quinoxyfen exceeded the LOC for mysid shrimp and Eastern oyster (airblast application to stone fruit), but not for saltwater diatom (Appendix I, Table 17). Thus, there is a potential risk to marine/estuarine invertebrates exposed to quinoxyfen through spray drift from airblast application. Refined risk quotients based on runoff inputs did not exceed the LOC indicating that a risk to marine/estuarine organisms is not expected from quinoxyfen runoff (Appendix I, Table 18).

4.2.3 Incident Reports

Environmental incident reports are obtained from two main sources, the Canadian pesticide incident reporting system (including both mandatory reporting from the registrant and voluntary reporting from the public and other government departments) and the United States Environmental Protection Agency Ecological Incident Information System (EIIS). Specific information regarding the mandatory reporting system regulations that came into force 26 April 2007, under the *Pest Control Products Act* can be found at http://www.hc-sc.gc.ca/cps-spc/pest/part/protect-proteger/incident/index-eng.php.

As of 12 August 2010, one incident was reported in the United States Environmental Protection Agency EIIS database. The incident occurred in California on 19 May 2008 and the causality was categorized as possible. The reported incident was for $300 plant damage following a direct treatment of Quintec Fungicide to a cherry orchard. There was no additional information about the rate of application or percent damage. The PMRA concluded that the information from the incident did not impact the risk assessment.

5.0 Value

5.1 Effectiveness Against Pests

5.1.1 Acceptable Efficacy Claims

5.1.1.1 Control of Powdery Mildew Caused by *Podosphaera clandestina* on Stone Fruits

Four trials conducted in the United States (WA) were submitted to support the claim for control of powdery mildew caused by *P. clandestina* on sweet cherries. Results from trials showed that Quintec Fungicide provided up to 100% control of powdery mildew when applied under low to moderate disease pressure at rates ranging from 439 to 585 mL/ha. Quintec Fungicide performed as well as the commercial standard. The claim for control of *P. clandestina* is extrapolated from sweet cherries to other stone fruits since that pathogen also attacks other stone fruits.

5.1.1.2 Suppression of Powdery Mildew Caused by *Sphaerotheca pannosa* on Stone Fruits

One trial on peach was conducted in the United States (WA). Quintec Fungicide provided 47% control of *S. pannosa* when applied at 585 mL/ha rate with four applications. Only the claim for suppression of powdery mildew caused by *S. pannosa* at the proposed rate of 500 mL/ha with five applications can be supported. The claim for control of *S. pannosa* is extrapolated from peach to other stone fruits since that pathogen also attacks other stone fruits.

5.1.1.3 Control of Powdery Mildew Caused by *Uncinula necator* on Grape

Results from three reviewed trials conducted in the United States (MI, NY, and OR) showed that Quintec Fungicide provided up to 94% control of powdery mildew when applied at rates of 293–439 mL/ha. The low tested rate of 293 mL/ha performed as well as the high tested rate of 439 mL/ha under high disease pressure. Therefore, the value for using the high proposed rate of 480 mL product/ha was not demonstrated. Only the low proposed rate (300 mL/ha) is supported.

5.1.1.4 Control of Powdery Mildew Caused by *Sphaerotheca macularis* on Strawberry

One trial conducted in Quebec was assessed. Results from the trial showed that Quintec Fungicide applied at the rates of 293 mL/ha and 439 mL/ha provided control of powdery mildew on strawberry. Quintec Fungicide performed better than the commercial standards.

5.1.1.5 Control of Powdery Mildew Caused by *Sphaerotheca fuliginea* on Melons, Pumpkin and Winter Squash

Four trials conducted on muskemelons (two trials) and on pumpkins (two trials) were reviewed. Results from trials showed that Quintec Fungicide applied at 293 mL/ha and 493 mL/ha provided up to 100% control of powdery mildew under moderate to high disease pressure. The claim for control of powdery mildew at the proposed rate of 300–400 mL/ha is extrapolated from muskemelons and pumpkins to melons and winter squash since the same pathogen also attacks these crops.

5.1.1.6 Control of Powdery Mildew Caused by *Erysiphe cichoracearum* on Head and Leaf Lettuce

Three trials were reviewed for the control of powdery mildew on lettuce. Quintec Fungicide applied at rates from 445 mL/ha to 474 mL/ha provided up to 100% control of powdery mildew under high disease pressure. In addition, lower rates than proposed (0.7–0.8X proposed rate) performed as well as the proposed rates. For these reasons, the claim for control of powdery mildew on head and leaf lettuce is supported at the rate of 240 mL/ha which is equivalent to 0.8X the lowest proposed rate (300 mL/ha).

5.1.1.7 Control of Powdery Mildew Caused by *Sphaerotheca fuliginea* on Hops

Efficacy of Quintec Fungicide to control *S. fuliginea* was demonstrated in strawberry efficacy trials. However, only the claim for suppression of powdery mildew is supported with a limit of two applications instead of four because of resistance management considerations. There is no other fungicide registered that can be alternated with Quintec Fungicide to control *S. macularis* on hops. With two applications Quintec Fungicide provided 67% control of *S. fuliginea.*

5.2 Phytotoxicity

No phytotoxicity was reported in any of the trials.

5.3 Economics

Not assessed.

5.4 Sustainability

5.4.1 Survey of Alternatives

A list of alternatives is available in Appendix I, Table 20.

5.4.2 Compatibility with Current Management Practices Including Integrated Pest Management

Not assessed.

5.4.3 Information on the Occurrence or Possible Occurrence of the Development of Resistance

Quinoxyfen belongs to Group 13 and is classified by the Fungicide Resistance Action Committee (FRAC) as a fungicide with medium resistance risk. The registration of Quintec Fungicide will provide growers with a new mode of action to control DMI-resistant prowdery mildew and will contribute to delaying further development of resistance to strobulurin fungicides.

5.4.4 Contribution to Risk Reduction and Sustainability

Not assessed.

6.0 Pest Control Product Policy Considerations

6.1 Toxic Substances Management Policy Considerations

The Toxic Substances Management Policy (TSMP) is a federal government policy developed to provide direction on the management of substances of concern that are released into the environment. The TSMP calls for the virtual elimination of Track 1 substances (those that meet all four criteria outlined in the policy: CEPA-toxic or equivalent, predominantly anthropogenic, persistent and bio-accumulative).

During the review process, quinoxyfen and its transformation products were assessed in accordance with the PMRA Regulatory Directive DIR99-03[5] and evaluated against the Track 1 criteria. The PMRA has reached the following conclusions:

- A preliminary review of the information indicates that quinoxyfen does not meet all Track 1 criteria and is not considered a Track 1 substance. Additional information is required to address uncertainties, in particular for 2-oxo-quinoxyfen. Comparison of available data for quinoxyfen against TSMP Track-1 criteria are shown in Table 19.
    - Quinoxyfen is persistent in soil under laboratory conditions and meets TSMP criteria for persistence.
    - In water, quinoxyfen does not meet TSMP criteria for persistence.
    - In air, quinoxyfen is not likely to meet TSMP criteria for persistence because of its low volatility.
    - As quinoxyfen meets persistence criterion in one media, then the criterion for persistence is considered to be met.
    - Although quinoxyfen meets numerical laboratory criteria indicating a potential for bioaccumulation, rapid depuration rates and field studies indicate that significant bioaccumulation under field conditions is unlikely.

[5] DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy.*

- Laboratory studies indicate that 2-oxo-quinoxyfen may meet the persistence criteria in soil and in sediment.
- The potential of 2-oxo-quinoxyfen to bioaccumulate is unknown. Additional confirmatory information is required to address uncertainties.

6.2 Formulants and Contaminants of Health or Environmental Concern

During the review process, contaminants in the technical and formulants and contaminants in the end-use products are compared against the *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* maintained in the *Canada Gazette*[6]. The list is used as described in the PMRA Notice of Intent NOI2005-01[7] and is based on existing policies and regulations including DIR99-03 and DIR2006-02[8], and taking into consideration the

Ozone-depleting Substance Regulations, 1998, of the *Canadian Environmental Protection Act* (substances designated under the Montreal Protocol). The PMRA has reached the following conclusions:

> Technical grade quinoxyfen and the end-use product Quintec Fungicide do not contain any formulants or contaminants of health or environmental concern identified in the *Canada Gazette*.
>
> The use of formulants in registered pest control products is assessed on an ongoing basis through PMRA formulant initiatives and Regulatory Directive DIR2006-02[9].

7.0 Summary

7.1 Human Health and Safety

The toxicology database submitted for quinoxyfen is adequate to define the majority of toxic effects that may result from exposure to quinoxyfen. In repeated dose toxicity studies on laboratory animals, the primary target of toxicity was the liver in all tested species and the hemolytic system in dogs. There was no evidence of cancer in mice or rats. Sensitivity of the young was not observed in the developmental toxicity studies. There was an increase in abortions in the rabbit developmental toxicity study at a maternally toxic dose which was also the highest dose tested. In the reproductive toxicity study, a marginal decrease in pup body weights was observed during lactation in the absence of adverse effects in the parents, and was

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6 *Canada Gazette*, Part II, Volume 139, Number 24, SI/2005-114 (2005-11-30) pages 2641–2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* and in the order amending this list in the *Canada Gazette*, Part II, Volume 142, Number 13, SI/2008-67 (2008-06-25) pages 1611-1613. *Part 1 Formulants of Health or Environmental Concern, Part 2 Formulants of Health or Environmental Concern that are Allergens Known to Cause Anaphylactic-Type Reactions and Part 3 Contaminants of Health or Environmental Concern.*

7 NOI2005-01, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern under the New Pest Control Products Act.*

8 DIR2006-02, *Formulants Policy and Implementation Guidance Documen.t*

9 DIR2006-02, PMRA Formulants Policy.

considered to be of low toxicological concern. There was no evidence of reproductive toxicity, and quinoxyfen was not considered to be genotoxic or neurotoxic.

Mixer, loader and applicators handling Quintec Fungicide and workers re-entering treated areas are not expected to be exposed to levels of Quintec Fungicide that will result in an unacceptable risk when the product is used according to label directions. The personal protective equipment on the product label is adequate to protect workers.

The nature of the residue in plants is adequately understood. The residue definition for enforcement purposes is quinoxyfen. The use of quinoxyfen on crops listed on the label and the import of quinoxyfen-treated commodities does not constitute an unacceptable dietary risk (food and drinking water) to any segment of the population, including infants, children, adults and seniors. Sufficient crop residue data have been reviewed to recommend maximum residue limits to protect human health.

7.2 Environmental Risk

There are no short term concerns with quinoxyfen affecting earthworms, birds, wild mammals and aquatic or terrestrial plants. The risk from exposure to beneficial arthropods and to bees from exposure by ingestion is unknown. As a precaution, statements for bees and beneficial arthropods will be added on the label. There are no short term concerns about the use of quinoxyfen affecting fish, amphibians, aquatic invertebrates and algae. Risks to aquatic organisms as a result of spray drift have been identified for aquatic habitats adjacent to the treatment area. To mitigate risks from the use of quinoxyfen to non-target aquatic organism, spray buffer zones are required for freshwater and marine habitats adjacent to the treatment area. The sizes of the buffer zones range from 1 to 20 meters for application rates ranging from 240 to 625 g a.i./ha. No risk from runoff to any aquatic species has been identified.

Additional data have been requested to assess the risk of quinoxyfen exposure to bees and beneficial arthropods. Additional data have also been requested to assess the chronic risk of 2-oxo-quinoxyfen to aquatic organisms.

Environmental risk will be revisited when all the requested data have been submitted.

7.3 Value

The efficacy and value evidence submitted to register Quintec Fungicide was sufficient to support the following uses:

- control of powdery mildew on head and leaf lettuce, grape, melon, pumpkin, winter squash and strawberry,
- control (*Podosphaera clandestina*) or suppression (*Sphaerotheca pannosa*) of powdery mildew on stone fruits, and
- suppression of powdery mildew on hops.

7.4 Unsupported Uses

Appendix I, Table 21 summarizes the supported and unsupported claims.

8.0 Regulatory Decision

Health Canada's PMRA, under the authority of the *Pest Control Products Act* and Regulations, has granted conditional registration for the sale and use of Quinoxyfen Technical Fungicide and Quintec Fungicide, containing the technical grade active ingredient quinoxyfen, to control powdery mildew on several fruits and vegetables.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

Although the risks and value have been found acceptable when all risk-reduction measures are followed, as a condition of these registrations, additional scientific information is being requested from the applicant for quinoxyfen. For more details, refer to the Section 12 Notice associated with these conditional registrations. The applicant will be required to submit this information.

NOTE: The PMRA will publish a consultation document at the time when there is a proposed decision on applications to convert these conditional registrations to full registrations or on applications to renew the conditional registrations, whichever occurs first.

Human Health

- Information on the toxicity of 2-oxo-quinoxyfen is required to characterize the potential risk to individuals exposed to 2-oxo-quinoxyfen through the consumption of groundwater. As a condition of registration, a valid rationale comparing the toxicity of 2-oxo-quinoxyfen to the parent, including any available toxicology data on 2-oxo-quinoxyfen must be provided.

Environment

For the parent compound quinoxyfen

- DACO 9.2.4.2 Acute oral toxicity study on bees
- DACO 9.2.5 Acute toxicity study on predators *(Typhlodromus pyri)*
- DACO 9.2.6 Acute toxicity study on parasites *(Aphidius rhopalosiphi)*

For the transformation product 2-oxo-quinoxyfen

Tier 1

- DACO 8.6 Other studies/Data/Reports (K_{ow} study)
- DACO 9.5.3.1 Fish, Early Life Cycle Toxicity Test

Tier 2 (based on the study results to be provided at Tier 1)

- DACO 9.5.3.2 Fish Full Life Cycle Toxicity Test with 2-oxo-quinoxyfen
- Mesocosm study to address bioaccumulation and fate potential of quinoxyfen and 2-oxo-quinoxyfen

List of Abbreviations

4-FP	4-fluorophenol
µg	microgram(s)
a.i.	active ingredient
ACN	acetonitrile
AD	administered dose
ADF	acid detergent fibre
ADI	acceptable daily intake
ALK	alkaline phosphatase
amu	atomic mass unit
AR	applied radioactivity
BAF	Bioaccumulation Factor
BBCH	a decimal code for the growth stages of cereals
BCF	Bioconcentration Factor
bw	body weight
BWG	body weight gain
CAF	composite assessment factor
CAS	chemical abstracts service
CBI	confidential business information
CEPA	*Canadian Environmental Protection Act*
CFBPQ	2-chloro-10-fluoro(1)benzopyrano(2,3,4-de)quinoline
cm	centimetres
cm^2	centimetre(s) squared
d	day(s)
DACO	data code
DALA	days after last application
DAT	days after treatment
DCHQ	5,7-dichloro-4-hydroxyguinoline
DFR	dislodgeable foliar residue
DMI	demethylation-inhibitor
DT_{50}	dissipation time 50% (the dose required to observe a 50% decline in concentration)
dw	dry weight
E_BC_{50}	concentration at which 50% reduction of biomass is observed
EC_{50}	effective concentration on 50% of the population
EC_{25}	effective concentration on 25% of the population
EDE	estimated daily exposure
EEC	estimated environmental exposure concentration
EIIS	Ecological Incident Information System
ELS	early life stage
EP	end-use product
F_{1a}	first litter of offspring descended from the adults that start the study (parental generation)
F_{1b}	second litter of offspring descended from the adults that start the study (parental generation)
F_2	first litter of the second offspring generation; descended from F_1 generation

FIR	food ingestion rate
FRAC	Fungicide Resistance Action Committee
fw	fresh weight
g	gram(s)
GC-MSD	gas chromatography with mass-selective detection
GC-MS/MS	tandem mass spectrometry
h	hour(s)
HDPE	high-density polyethylene
ha	hectare(s)
HAFT	highest average field trial
HPLC	high performance liquid chromatography
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram(s)
K_{oc}	organic-carbon partition coefficient
K_{ow}	*n*–octanol-water partition coefficient
L	litre(s)
LC_{50}	lethal concentration 50%
LD	low dose
LD_{50}	lethal dose 50%
LOAEL	lowest observed adverse effect level
LOC	level of concern
LOD	limit of detection
LOQ	limit of quantification
M	mole(s)
MAS	maximum average score
Max	maximum
mg	milligram(s)
MI	Michigan state
Min	minimum
Min.	minute(s)
MIS	maximum irritation score
mL	millilitre(s)
MOE	margin of exposure
MRL	maximum residue limit
n	number of test subjects
NA	not available
NAFTA	North American Free Trade Agreement
nm	nanometre(s)
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
NY	New York state
ON	Ontario
OR	Oregon state
Pa	Pascal(s)
PCPA	*Pest Control Product Act*
PET	polyethylene terephthalate

PHED	Pesticide Handlers Exposure Database
PHI	preharvest interval
p*K*a	dissociation constant
PMRA	Pest Management Regulatory Agency
ppb	parts per billion
ppm	parts per million
RQ	risk quotient
RTI	retreatment interval
SFO	single first-order kinetics
$t_{1/2}$	half-life
TP	transformation product
TRR	total radioactive residue
TSMP	Toxic Substances Management Policy
Std. Dev.	Standard deviation
URMUR	User Requested Minor Use Registration
uv	ultraviolet
WA	Washington state

Appendix I Tables and Figures

Table 1 Residue Analysis

Matrix	Method ID	Analyte	Method Type	LOQ		Reference
Plant	ERC 95.26 Enforcement method	Active	GC-MSD (gas chromatography with mass-selective detection)	0.01 ppm	Grapes, grape juice, raisins, wine, grape must, cherries	779404, 779405, 779406
				0.05 ppm	Grape pomace, hops	
Soil / Sediment	DowElanco Analytical Method ERC 94.27	Active	GC-MSD 237 amu, 272 amu	10 ppb	Loamy silt Loamy sand Sandy clay loam	1642947, 1642948, 1642949
		Metabolite 1	GC-MSD 337 amu, 330 amu	10 ppb	Loamy silt Loamy sand Sandy clay loam	
Soil / Sediment	Dow AgroSciences LLC Analytical Method GRM 00.16	Active	GC-MS/MS 307 amu 272 amu	5.8 ppb	Unknown soil types	1642950
		Metabolite 1	GC-MS/MS 380 amu 344 amu	5.9 ppb		
		Metabolite 2	GC-MS/MS 270 amu 206 amu	3.7 ppb		
Water	DowElanco Europe Study ID ERC 95.14	Active	HPLC/UV	0.5 ppb	Drinking water	1642952
Water	DowElanco Europe Study ID ERC 95.18	Active	GC-MSD 237 amu 272 amu	1.0 ppb	Surface water	1642953
Water		Metabolite 2	GC-MSD 270 amu 234 amu			
Water	ABC Laboratories Protocol No. AA8702, Study # 42537	Active	HPLC/UV	4.32 ppb	Fresh aquatic test water	1642955

Active: quinoxyfen; 5,7-dichloro-4-(4-fluorophenoxy)quinoline
Metabolite 1: 3-hydroxy quinoxyfen; 5,7-dichloro-4-(4-fluorophenoxy)-3-quinolinol
Metabolite 2: 5,7-dichloro-4-quinolinol

Table 2 Acute Toxicity of Quinoxyfen and Its Associated End-use Product (Quintec Fungicide)

Study Type	Species	Result	Comment	Reference
Acute Toxicity of Quinoxyfen (Technical)				
Oral	Rat	LD_{50} >5000 mg/kg bw	Low Toxicity	779432-779433
Dermal	Rabbit	LD_{50} >2000 mg/kg bw	Low Toxicity	779434
Inhalation	Rat	LC_{50} >3.38 mg/L	Low Toxicity	779435
Skin irritation	Rabbit	MIS = 0/8 MAS (24, 48 and 72 h) = 0/8	Non-irritating	779437
Eye irritation	Rabbit	MIS=7.2/110 at 1 h MAS (24, 48 and 72 h) = 1.3/110	Mildly irritating "CAUTION EYE IRRITANT"	779436
Skin sensitization (Maximization)	Guinea pig	Skin sensitizer	Potential skin sensitizer "POTENTIAL SKIN SENSITIZER"	779438
Skin sensitization (Buehler)	Guinea pig	Not a skin sensitizer	Not a skin sensitizer	779439
Acute Toxicity of End-Use Product – Quintec Fungicide				
Oral	Rat	LD_{50} >5000 mg/kg bw	Low Toxicity	779388
Oral	Rat	LD_{50} >2000 mg/kg bw	Low Toxicity	779389
Dermal	Rat	LD_{50} >5000 mg/kg bw	Low Toxicity	779390
Dermal	Rat	LD_{50} >2000 mg/kg bw	Low Toxicity	779392
Inhalation	Waiver was accepted based on the low acute toxicity of the active ingredient and the high viscosity of the test substance.			779393, 779394
Skin irritation	Rabbit	MAS = 0.67/8	Slightly irritating	779397
Skin irritation	Rabbit	MAS = 0/8	Non-irritating	1771822
Eye irritation	Rabbit	MIS = 13.7/110 (1 h) MAS = 1.78/110 (24, 48, 72 h)	Minimally irritating	779395
Eye irritation	Rabbit	MIS = 1.33/110 (1 h) MAS = 0/110 (24, 48, 72 h)	Minimally irritating	779396
Skin sensitization (Buehler)	Guinea pig	Not a skin sensitizer	Not a skin sensitizer	779401-779402
Skin sensitization (Buehler)	Guinea pig	Not a skin sensitizer	Not a skin sensitizer	779398, 779399

a MAS = maximum average score for 24, 48 and 72 hours

b MIS = maximum irritation score

Table 3 Toxicity Profile of Quinoxyfen Technical

Study Type	Species	Results[a] (mg/kg/day in Males/Females)	Reference
28-day dermal toxicity	Rat	Dermal irritation: No treatment related effects were observed at any dose. NOAEL: 1000 LOAEL was not determined. There were no treatment-related effects.	779450, 940762
28-day dietary (supplemental)	Rat	Effect levels were not established since this study was considered to be supplemental. Treatment-related effects consisted of decreased body weight/gains and food consumption at lower doses, and testicular effects (atrophic testes, decreased spermatogenesis) at a limit dose.	779444
28-dietary (supplemental)	Dog	Effect levels were not established since this study was considered to be supplemental. Treatment-related effects consisted of decreased body weight/gains, food consumption and slight hepatocyte vacuolation in the liver.	779446
30-day dietary (supplemental; non-guideline)	Dog	Effect levels were not established since this study was considered to be supplemental. Treatment-related effects consisted of decreased body weight/gains, food consumption and increased hepatocyte vacuolation and necrosis in the liver at lower doses. At the high dose, decreased red blood cell parameters (females), small thymuses and testes, and renal proximal tubule vacuolation were observed.	779445
90-day dietary	Mouse	NOAEL: 100 LOAEL: 500, based on increased liver weights, hepatocellular hypertrophy and individual hepatocyte necrosis.	779440-779441
90-day dietary	Rat	NOAEL: 253/10 LOAEL: not established/100, based on decreased body weight/gains (females), increased liver weights, hepatocellular hypertrophy with basophilia.	779442-779443
90-day dietary	Dog	NOAEL: 100 LOAEL was not determined. There were no treatment-related effects.	779447-779448
1-year dietary	Dog	NOAEL: 20 LOAEL: 200, based on one male mortality due to hemolytic anemia, decreased body weight/gains and food consumption, increased liver weights, increased ALK activity, haemolytic anemia associated with increased hematopoiesis in bone marrow and spleen, increased size of hepatocytes sometimes accompanied with increased bile canaliculi and extramedullary hematopoiesis in the spleen.	779449
Carcinogenicity (18-month dietary)	Mouse	NOAEL: 80 LOAEL: 250, based on decreased body weight gains (both sexes) and food efficiency (female). **No evidence of carcinogenicity.**	779452, 940806, 940808, 940897, 940899

Study Type	Species	Results[a] (mg/kg/day in Males/Females)	Reference
Chronic/ Carcinogenicity (2-year dietary)	Rat	NOAEL: 20 LOAEL: 80, based on decreased body weight gains, food consumption, moderate chronic progressive glomerulonephropathy (males), roughened kidney surface and chronic progressive nephropathy (males). **No evidence of carcinogenicity.**	779451, 940780-940792, 940801
Two-generation reproduction	Rat	**Parental toxicity**: NOAEL: 100 LOAEL was not determined. There were no treatment-related effects. **Offspring toxicity:** NOAEL: 20 LOAEL: 100, based on decreased pup body weight and body weight gains during lactation. **Reproductive toxicity:** NOAEL: 100 LOAEL was not determined. There were no treatment-related effects. **No evidence of reproductive toxicity.**	779453, 941098, 941100, 941102
Developmental toxicity	Rat	**Maternal:** NOAEL: 1000 LOAEL was not determined. There were no treatment-related effects. **Developmental:** NOAEL: 1000 LOAEL was not determined. There were no treatment-related effects. **No evidence of teratogenicity or increased susceptibility of fetuses compared to adults.**	779454
Developmental toxicity (supplemental range-finding)	Rabbit	Effect levels were not established since this study was considered to be supplemental. Treatment-related effects consisted of decreased maternal body weight/gains, food consumption and maternal mortalities. The maximum tolerated dose was exceeded.	779455
Developmental toxicity	Rabbit	**Maternal:** NOAEL: 80 LOAEL: 200, based on increased clinical signs (decreased fecal output, soft feces, perineal soiling, blood or urine contained blood in the cage pan), decreased body weight gains and food consumption. **Developmental:** NOAEL: 80 LOAEL: 200, based on increased fetal loss (abortions). **No evidence of teratogenicity or increased susceptibility of fetuses compared to adults.**	779455-779456

Study Type	Species	Results[a] (mg/kg/day in Males/Females)	Reference
Reverse gene mutation assay	*Salmonella typhimurium strains, E. coli*	Negative	779461
Gene mutations in mammalian cells in vitro	Chinese hamster ovary cells	Negative	779457
In vitro mammalian chromosomal aberration	Rat lymphocytes	Negative	779458
In vivo mammalian cytogenetics	Mice	Negative	779459-779460
Acute neurotoxicity (gavage)	Rat	NOAEL: 2000 LOAEL not determined. There were no treatment-related effects. **No evidence of neurotoxicity.**	779464, 941108, 941110
1-year neurotoxicity (dietary)	Rat	Systemic NOAEL: 80/20 Systemic LOAEL: not determined/80, based on decreased body weight gains in females. Neurotoxicity NOAEL: 80 Neurotoxicity LOAEL was not determined. There were no treatment-related neurotoxic effects. **No evidence of neurotoxicity.**	779465, 941112
Metabolism	Rat	**Absorption:** Quinoxyfen was rapidly absorbed and excreted. The feces represented the major route of elimination as 68–78% of the dose was eliminated via this route in 48 h, whereas, 13–29% was eliminated in the urine. The tissues and carcass accounted for 1–7%, gastrointestinal tract <3% and final cage wash <1% of the AD. **Distribution:** The highest concentration of radioactivity was found in the fat followed by the ovaries, liver, kidney, gastrointestinal tract and carcass. Overall, concentration of the radioactivity in tissues was very low (≤1%) and was comparable between the doses and sexes. There was no evidence of bioaccumulation. **Metabolism:** Quinoxyfen was extensively metabolized. ≤3% of radioactivity in the blood was found to be associated with parent compound, indicating a high first pass metabolism. The major metabolites identified in urine resulted from extensive cleavage of the diaryl-ether linkage of quinoxyfen resulting in formation of acid-labile conjugates of 4-fluorophenol (4-FP) and 5,7-dichloro-4-hydroxyguinoline (DCHQ) and lesser quantities of free DCHQ and 4-FP. The major metabolites found in bile were glucuronide and/or sulfate conjugates of two isomers of fluorophenyl ring-hydroxy-quinoxyfen. No parent compound was found in urine and only a trace detected in the bile. Feces contained parent compound and unconjugated forms of the same two isomers of fluorophenyl ring-hydroxy-quinoxyfen were seen in the bile. There were no apparent differences in the metabolism and disposition of quinoxyfen between the sexes or single and repeated exposure.	779462, 779463

a Effects observed in males as well as females unless otherwise reported

Table 4 Toxicology Endpoints for Use in Health Risk Assessment for Quinoxyfen Technical

Exposure Scenario	Dose (mg/kg bw/day)	Study	Endpoint	CAF[1] or Target MOE[2]
Acute Dietary	Not required			
Chronic Dietary	NOAEL = 20	2-year rat combined chronic/ carcinogenicity study	Decreased body weight gains and food consumption in both sexes; chronic progressive glomerulonephropathy, increased blood urea nitrogen in blood and roughened kidney surface in males	100
	ADI = 0.2 mg/kg bw/day			
Short-term to Intermediate-term Dermal and Inhalation	NOAEL = 20	2-generation reproductive toxicity	Decreased pup body weights and overall pup body weight gain during lactation	100

[1] Dietary scenarios
[2] Occupational exposure scenarios

Table 5 Integrated Food Residue Chemistry Summary

NATURE OF THE RESIDUE IN PLANTS - CUCUMBER			**PMRA# 779471 and 877574**	
Radiolabel Position	**4-fluorophenoxy UL-ring-^{14}C and 2-^{14}C quinoline ring**			
Test site	Greenhouse			
Treatment	Foliar spray			
Rate	5.9 mg a.i./plant until run-off			
Timing	At start of fruit ripening, then at 10 and 23 days after initial treatment			
Preharvest interval	7 days			
End-use product	Formulated as a suspension concentrate			
The total radioactive residues (TRRs; expressed as quinoxyfen equivalents) in/on mature cucumber fruits were 0.079 ppm (phenyl label) and 0.076 ppm (quinoline label). In mature foliage, the TRRs were 4.218 ppm (phenyl label) and 3.399 ppm (quinoline label). In cucumber fruits, approximately 77% of the TRRs (phenyl label) and 67% of the TRRs (quinoline label) were identified. In cucumber foliage, approximately 79% of the TRRs (phenyl label) and 60% of the TRRs (quinoline label) were identified. Overall accountabilities were 106.7% and 108.5% for phenyl-labeled cucumber fruit and foliage, respectively, and 111.3% and 99.0% for quinoline-labeled cucumber fruit and foliage, respectively.				
Metabolites Identified	**Major Metabolites (> 10% TRR)**		**Minor Metabolites (< 10% TRR)**	
Radiolabel Position	**Phenyl**	**Quinoline**	**Phenyl**	**Quinoline**
Cucumber fruit	Quinoxyfen	Quinoxyfen	Quinoxyfen n-oxide	Quinoxyfen n-oxide
Cucumber foliage	Quinoxyfen	Quinoxyfen	Quinoxyfen n-oxide, 2-oxo quinoxyfen	Quinoxyfen n-oxide, 2-oxo quinoxyfen
NATURE OF THE RESIDUE IN PLANTS - TOMATO			**PMRA# 779417**	
Radiolabel Position	**4-fluorophenoxy UL-ring-^{14}C and 2-^{14}C quinoline ring**			
Test site	Outdoor plots			
Treatment	Foliar spray			

Rate	0.11-0.12 kg a.i./ha for total of ~0.6 kg a.i./ha
Timing	First to plant bearing immature fruits or 6 weeks prior to mature harvest. Subsequent applications at 7-day RTI
Preharvest interval	Mature fruit and foliage collected 14 days after fifth application
End-use product	Formulated as a suspension concentrate

The total radioactive residues (TRRs; expressed as quinoxyfen equivalents) in/on mature samples of tomatoes were 0.191 ppm (phenyl label) and 0.243 ppm (quinoline label). In foliage, the TRRs were 10.716 ppm (phenyl label) and 14.112 ppm (quinoline label). Surface rinsing released approximately 57–62% of the TRRs in mature tomatoes and 41–49% of the TRRs in foliage.

Radioactive residues in/on post-rinsed samples were extracted sequentially, as needed, with neutral solvents and acid reflux with an acetonitrile (ACN) extract. The surface rinses, extracts, and hydrolysates were analysed by chromatographic techniques. In tomato fruits, >71–74% of the TRRs were identified and characterized. In tomato foliage, >62–67% of the TRRs were identified/characterized. With additional foliage samples, fractionation and isolation procedures were used to characterize low-level unknowns. The unknowns were tentatively identified as CFBPQ (2-chloro-10-fluoro(1)benzopyrano(2,3,4-de)quinoline), the 3-OH metabolite, and the *p*-hydroxyphenoxy metabolite.

Bound residues were subjected to hydrolysis and acid detergent fibre (ADF) procedures to determine whether residues are associated with natural constituents. The procedures showed that the majority of the bound residues were associated with ADF (10–12% of the TRRs in fruits and 3.7–4.6% of the TRRs in foliage) containing lignin, cellulose, and hemicellulose. The remaining non-extractable residues following extraction, hydrolysis, and ADF procedures were less than 0.01 ppm.

Metabolites Identified	**Major Metabolites (> 10% TRR)**		**Minor Metabolites (< 10% TRR)**	
Radiolabel Position	**Phenyl**	**Quinoline**	**Phenyl**	**Quinoline**
Tomato fruit	Quinoxyfen	Quinoxyfen	–	–
Tomato foliage	Quinoxyfen	Quinoxyfen	4-fluorophenol	–

NATURE OF THE RESIDUE IN PLANTS – SUGAR BEET	**PMRA# 779416 and 939288**
Radiolabel Position	**4-fluorophenoxy UL-ring-^{14}C and 2-^{14}C quinoline ring**
Test site	Outdoor plots
Treatment	Foliar spray
Rate	348–361 g a.i./ha/season; 588–646 g a.i./ha exaggerated study
Timing	First at BBCH 39 growth stage; second 60 days later or ~26 days prior to mature harvest
Preharvest interval	0, 7, 14, 28 days after first application or 26 days after last application
End-use product	Formulated as a suspension concentrate

The total radioactive residues (TRRs), expressed as quinoxyfen equivalents in/on mature sugar beet root samples were 0.078 ppm (phenyl label) and 0.049 ppm (quinoline label). In treated sugar beet tops, the TRRs were 1.892 ppm (phenyl label) and 2.205 ppm (quinoline label). The lower TRRs in roots suggest that there was little translocation of radioactivity from the tops (leaves) to the roots.

Residues in sugar beet matrices were repeatedly extracted with acetonitrile:water. Extractable residues in sugar beet roots accounted for 76.8% of the TRRs (phenyl label) and 68.0% of the TRRs (quinoline label); 74.1% of the TRRs (phenyl label) and 54.8% of the TRRs (quinoline label) in sugar beet tops. Chromatographic analyses of the acetonitrile:water extract showed the nature of radioactivity to be similar between the phenyl and quinoline labels.

To further characterize the unidentified polar metabolites, acid hydrolysis and multiple liquid-liquid partitioning were attempted and results were averaged. The non-extractable residues, after initial extraction of samples with acetonitrile:water, were 23.2–32.0% of the TRRs (roots) and 17.8–35.9% of the TRRs (tops). No further attempts were made to characterize bound residues in roots since the TRRs were ≤0.02 ppm. To characterize bound residues in sugar beet tops, subsamples were subjected to acid detergent fiber, cellulose, and lignin isolation

procedures. The results of these procedures showed that most of the radioactivity was associated with lignin.				
Metabolites Identified	**Major Metabolites (> 10% TRR)**		**Minor Metabolites (< 10% TRR)**	
Radiolabel Position	**Phenyl**	**Quinoline**	**Phenyl**	**Quinoline**
Sugar beet tops	Quinoxyfen, 4-fluorophenol	Quinoxyfen	CFBPQ	DCHQ, CFBPQ
Sugar beet roots	Quinoxyfen	Quinoxyfen	–	–

NATURE OF THE RESIDUE IN PLANTS – GRAPE	**PMRA# 779470**
Radiolabel Position	**4-fluorophenoxy UL-ring-^{14}C and 2-^{14}C quinoline ring**
Test site	Greenhouse
Treatment	Foliar spray
Rate	0.33–0.52 mg a.i./bunch to run-off or 0.62–0.76 mg a.i./bunch
Timing	Early application: 18 days after the end of flowering Late application: 5 weeks after the first application
Preharvest interval	0, 15, 30 and 45 days (maturity) - early application; 0, 10 days- late application
End-use product	Formulated as a suspension concentrate

Samples were sequentially washed with water, dichloromethane and methanol, and levels of radioactivity were determined in the washes and fruits. At all sampling intervals, the majority of total radioactive residues (81–99% of the TRRs) was removed by surface washing. Following surface washing, residues in/on fruits were extracted with organic solvents. The TRRs, expressed as quinoxyfen equivalents, in/on treated mature grapes declined at each successive sampling interval. For the early treatment samples harvested at PHIs of 0, 30 and 45 days, residues declined from 13.30 ppm to 2.513 ppm (phenyl label) and from 9.121 ppm to 1.985 ppm (quinoline label). For the late treatment, residues declined from 4.857 ppm to 2.907 ppm (phenyl-label) and 4.954 ppm to 4.235 ppm (quinoline-label) after 10 days.

The nonextractable residues of grapes treated at the 'early stage' were subjected to mild base hydrolysis, releasing an additional 1.2–2.0% of the TRRs. Bound residues remaining following surface washing, simple extraction, and/or base hydrolysis accounted for 1.2–4.6% of the TRRs. Accountabilities were 100.2–103.1% for phenyl- and quinoline-labelled mature grapes, treated at the early or later growth stage.

Additionally, the radiolabelled test substances were applied as a direct spray to the fruits of established grape plants at a rate of 750 mg a.i./L (0.62–0.76 mg a.i./bunch). Residues in/on washed mature fruits were extracted with organic solvents. The TRRs were 6.672 ppm (phenyl label) and 5.273 ppm (quinoline label). The distribution of radioactivity between the various surface washes and fruits was similar to that observed for the lower treatment rate. The proportions of quinoxyfen, unidentified polar materials, and nonextractable residues were also similar.

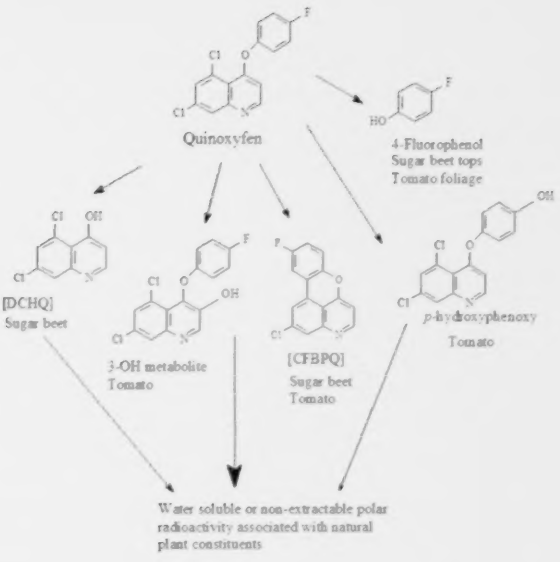
A separate translocation experiment was conducted. The test substances were directly applied to the part of a whole vine at 375 mg a.i./L. Residues did not appear to translocate from treated vines to untreated sections of the plant. Metabolic profiles were similar for both phenyl- and quinoline-labelled grape and vine samples, with quinoxyfen identified as the primary residue; however, quinoxyfen appears to be more metabolized in vines than grapes, based on higher levels of polar and unidentified components, and bound residues in vines.

Metabolites Identified	**Major Metabolites (> 10% TRR)**		**Minor Metabolites (< 10% TRR**	
Radiolabel Position	**Phenyl**	**Quinoline**	**Phenyl**	**Quinoline**
Grape	Quinoxyfen	Quinoxyfen	–	–

NATURE OF THE RESIDUE IN PLANTS – WINTER WHEAT			PMRA# 779468 and 927812	
Radiolabel Position	**4-fluorophenoxy UL-ring-^{14}C and 2-^{14}C quinoline ring**			
Test site	Outdoor plots			
Treatment	Foliar spray			
Rate	250 g a.i./ha (low); 1000 g a.i./ha (high)			
Timing	Early: at BBCH 32 growth stage; Late: ~4 weeks later, to separate plants at BBCH 49 growth stage			
Preharvest interval	0, 14, 29, 105 days -early application 1, 78 days- late application			
End-use product	Formulated as an emulsifiable concentrate			
The total radioactive residues (TRRs; expressed as quinoxyfen equivalents) in/on mature wheat grain samples were 0.036 ppm (phenyl label) and 0.057 ppm (quinoline label). In mature wheat straw, the TRRs were 2.073 ppm (phenyl label) and 4.376 ppm (quinoline label). The metabolism of quinoxyfen in forage was qualitatively the same as in straw. In wheat grain, the TRRs were low and extractable residues were only 9.82% of the TRRs (phenyl label) and 8.94% of the TRRs (quinoline label). Subsamples of mature wheat grain were subjected to additional fractionation procedures to investigate the possible incorporation of residues into natural products such as starch. Approximately 13% and 53% of the TRRs were determined to be associated with starch in phenyl- and quinoline-labelled grain, respectively. In wheat straw, extractable residues were 35.44% of the TRRs (phenyl label) and 25.66% of the TRRs (quinoline label). Efforts to characterize Metabolite A demonstrated that it did not consist of parent or related compounds conjugated to naturally-occurring compounds but was composed of small organic acids. Samples of wheat straw were subjected to several fractionation procedures in attempts to further characterize bound residues. Considering the results from three different lignin/cellulose procedures, it was concluded that at least 15% and 20% of the wheat straw TRRs are associated with lignin, and at least 24% and 29% of the TRRs are associated with cellulose in phenyl- and quinoline-labelled straw, respectively. For grain, accountabilities were 94.2% and 93.2% of the TRRs for phenyl and quinoline labels, respectively. For straw, accountabilities were 101.7% and 75.2% of the TRRs for phenyl and quinoline labels, respectively.				
Metabolites Identified	**Major Metabolites (> 10% TRR)**		**Minor Metabolites (< 10% TRR)**	
Radiolabel Position	**Phenyl**	**Quinoline**	**Phenyl**	**Quinoline**
Winter wheat grain	–	–	Quinoxyfen, Metabolite A	Quinoxyfen, Metabolite A
Winter wheat straw	Quinoxyfen, Metabolite A	Metabolite A	–	Quinoxyfen
CONFINED ROTATIONAL CROP STUDY USING CABBAGE, TURNIP AND SUNFLOWER			**PMRA# 779469**	
Radiolabel Position	**Fluorophenoxy UL-^{14}C and 2-^{14}C quinoline**			
Test site	Greenhouse in England			
Treatment	Hand sprayer			
Rate	400 g a.i./ha			
Timing	Bare soil			
Plantback interval	30 days			
End-use product	Emulsifiable concentrate			
In a confined rotational crop study, phenyl- or quinoline-ring labeled [^{14}C]quinoxyfen was applied as a spray solution to the surface of a sandy loam soil at 400 g a.i./ha. Cabbage (leafy vegetable), turnip (root crop) and				

sunflower (seed crop) were planted onto the treated soil 30 days after application of the test substances. The crops were allowed to grow according to typical agricultural practices. The total radioactive residues (TRRs; expressed as quinoxyfen equivalents) were all below 0.01 ppm in/on all raw agricultural commodities collected (turnip root, cabbage leaves and sunflower head) at the 30-day plantback interval; therefore, the treated samples were not further analyzed.

Proposed metabolic scheme in plants



In cucumber and tomato, unchanged quinoxyfen remained largely on the surface of treated plants. The presence of multiple unidentified polar residues suggests that metabolism of quinoxyfen does occur to some extent to form more polar soluble components with the incorporation into insoluble material, such as lignin and cellulose. Quinoxyfen appears to be metabolized in sugar beets to some extent and may then be incorporated with natural plant constituents such as lignin. The initial breakdown of quinoxyfen on leaves may result from surface photolysis and resulting photo-degradates may be further metabolized to polar residues. In addition, the ether bond of the quinoxyfen compound may be broken during metabolism yielding the 4-fluorophenol and DCHQ metabolites.

CROP FIELD TRIALS ON STONE FRUITS	**PMRA# 779411, 779412, 1771827 and 1771828**

Seven trials on tart cherries (one trial each in Zones 1, 9 and 11, and four trials in Zone 5) and six trials on sweet cherries (two trials each in Zones 5, 10 and 11) were conducted in the United States during the 2000-2001 growing seasons. Eleven trials on peaches (one trial each in Zones 1, 5 and 6, four trials each in Zones 2 and 10) and six trials on plums (one trial each in Zones 5 and 12, and four trials in Zone 10) were conducted in the United States during the 2003 growing season. All applications were carried out with Quintec 250SC (EF-1295; 250 g/L quinoxyfen). In the cherry trials, five foliar applications were made at a rate of ~120 g a.i./ha, for a seasonal rate of 620 g a.i./ha. Cherries were harvested at pre-harvest intervals (PHIs) of 6–8 days. In the peach and plum trials, four foliar applications were made at a rate of ~146 g a.i./ha at 6–8 day intervals, for a total rate of 575–598 g a.i./ha. One additional application was made at one site in one peach trial in Zone 6 to allow the fruit to become mature, corresponding to a total rate of 725 g a.i./ha. Mature peach fruits were harvested at PHIs of 6–8 days. Mature plum fruit was harvested and pitted seven days after the final application.

Commodity	Total Rate (g a.i./ha)	PHI (days)	Quinoxyfen Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Cherry, sour	620	6–7	14	0.046	0.269	0.267	0.125	0.13	0.067
Cherry, sweet	620	7–8	12	0.03	0.146	0.141	0.114	0.1	0.039
Peach	575–598	6–8	20	0.063	0.540	0.475	0.095	0.150	0.123
	725	8	2	0.43	0.550	0.490	0.490	0.490	NA
Plum	578–585	7	12	<0.01	0.095	0.091	0.010	0.024	0.031

RESIDUE DECLINE IN STONE FRUITS — **PMRA# 1771829 and 1771832**

In one European peach trial and two European nectarine trials, fruit samples were harvested at 0, 1, 3, 7 and 13–14 days after last application (DALA). Mean residues in treated fruit samples decreased from 0.052 ppm (0 DALA) to <0.01 ppm (13 DALA) on peaches, and from 0.069 ppm (0 DALA) to 0.01 ppm (14 DALA) on nectarines.

CROP FIELD TRIALS ON CANTALOUPES — **PMRA# 1771825**

Eleven supervised crop field trials were conducted in the United States and Canada on cantaloupes during the 2001 growing season: one trial each in Zones 5, 5B and 12, two trials each in Zones 2 and 6, and four trials in Zone 10. In all trials except one, four foliar applications of Quintec 250SC (EF-1295; 250 g/L quinoxyfen) were made at a rate of ~146 g a.i./ha at 6–12 day intervals for a total rate of 581–619 g a.i./ha. In one trial, five applications were made due to cool weather conditions, for a total rate of 747 g a.i./ha. At all sites, cantaloupes were harvested 2–4 days after the final application.

Commodity	Total Rate (g a.i./ha)	PHI (days)	Quinoxyfen Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Cantaloupe	581–747	2–4	22	<0.01	0.056	0.050	0.028	0.030	0.01

RESIDUE DECLINE IN CANTALOUPES — **PMRA# 1771825**

Cantaloupe samples were harvested at 0, 2, 3, 4, 7 and 14 days after last application (DALA). Mean residues in samples of treated cantaloupe decreased from 0.052 ppm at 0 DALA to 0.015 ppm at 14 DALA.

CROP FIELD TRIALS ON GRAPES — **PMRA# 779414 and 941125**

Fifteen trials on grapes were conducted in the United States and Canada during the 1999 growing season: one trial in Zone 2, two trials each in Zones 1 and 5, three trials in Zone 11 and seven trials in Zone 10. At each trial location, five applications of Quintec 250SC (EF 1295; 250 g/L quinoxyfen) were made to grapes as directed foliar sprays at a rate of ~120 kg a.i./ha, for a total rate of 570–800 g a.i./ha. In the two Ontario trials, an additional plot was treated with five applications at a rate of 60 g a.i./ha/application, for a total of 300 g a.i./ha. In all trials, the first application was made when grapes were at the fruiting stage, and subsequent applications were made at 6- to 8-day retreatment intervals (RTIs). Mature grapes were harvested 13–15 days following the last spray.

Commodity	Total Rate (g a.i./ha)	PHI (days)	Quinoxyfen Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Grapes	300	14	4	0.085	0.135	0.125	0.107	0.11	0.023
	570–800	13–15	30	0.048	0.480	0.437	0.150	0.17	0.1

RESIDUE DECLINE IN GRAPES — **PMRA# 1771834**

A residue decline trial on grapes was conducted in Southern France during the 1996 growing season at a rate of 62.5 g a.i./ha. Samples were harvested at 0, 5, 10, 15 and 21 DALA. Mean residues in samples of treated grapes decreased from 0.24 ppm at 0 DALA to 0.10 ppm at 21 DALA.

CROP FIELD TRIALS ON HOPS — **PMRA# 779413**

Three hop trials were conducted during the 1999 growing season in Zones 11 (two trials) and 12 (one trial). At each trial location, three or four applications of Quintec 250SC (EF-1295; 250 g/L quinoxyfen) were made to hops as directed foliar sprays for a total application rate of 590–760 g a.i./ha. The first application was made when hops were at the flowering stage, and subsequent applications were made at 11- to 20-day RTIs. Dried hop cones were harvested 20–21 days following the last spray schedule.

Commodity	Total Rate (g a.i./ha)	PHI (days)	Quinoxyfen Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Hops	590–760	20–21	6	0.384	2.46	2.16	1.22	1.26	0.82

CROP FIELD TRIALS ON LETTUCE — **PMRA# 1641969**

Supervised crop field trials were conducted in the United States during the 2002 growing season on head lettuce (eight total: one trial each in Zones 2, 3 and 8, and five trials in Zone 10) and leaf lettuce (eight total: one trial each in Zones 2, 3 and 8, and five trials in Zone 10). In 14 of the trials, four foliar applications of Quintec 250SC (EF-1295; 250 g/L quinoxyfen) were made at a rate of ~146 g a.i./ha at 5–9 day intervals for a total rate of 571–622 g a.i./ha. In two trials (one trial each on head and leaf lettuce), five applications were made due to cool weather conditions, for a total rate of 738–747 g a.i./ha. At all sites, head and leaf lettuce were harvested one day after the final application.

Commodity	Total Rate (g a.i./ha)	PHI (days)	Quinoxyfen Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Leaf lettuce	571–738	1	16	1.20	14.0	13.0	3.05	4.46	3.8
Head lettuce w/ wrapper leaves	582–747	1	16	0.80	5.80	5.30	1.97	1.30	1.5

RESIDUE DECLINE IN LETTUCE — **PMRA# 1771826**

Leaf lettuce samples were harvested at 1, 3–4, 7 and 14 days after last application (DALA). Mean residues in samples of treated lettuce decreased from 4.55 ppm at 1 DALA to 1.02 ppm at 14 DALA.

CROP FIELD TRIALS ON STRAWBERRIES — **PMRA# 1641968**

Eight supervised crop field trials were conducted in the United States on strawberries during the 2002 growing season: one trial each in Zones 3, 5 and 12, two trials in Zone 2, and three trials in Zone 10. In all trials, four foliar applications of Quintec 250SC (250 g/L quinoxyfen) were made at a rate of ~149 g a.i./ha at 6–8 day intervals for a total rate of 580–648 g a.i./ha. In all trials, the first application was made 20–22 days to harvest and mature strawberries were harvested one day after the final application.

Commodity	Total Rate (g a.i./ha)	PHI (days)	Quinoxyfen Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Strawberry	580–648	1	16	0.032	0.574	0.561	0.325	0.322	0.185

RESIDUE DECLINE IN STRAWBERRIES — **PMRA# 1641968**

Strawberry samples were harvested at 1, 3, 6–7 and 13–14 days after last application (DALA). Mean residues in samples of treated strawberries decreased from 0.431 ppm at 1 DALA to 0.048 ppm at 13–14 DALA.

CROP FIELD TRIALS ON WINTER SQUASH — **PMRA# 1771824**

Five supervised crop field trials were conducted in the United States on winter squash during the 2003 and 2004 growing seasons: one trial each in Zones 3, 5 and 10, and two trials in Zone 2. In all trials, four foliar applications of Quintec 250SC (EF-1295; 250 g/L quinoxyfen) were made at a rate of ~147 g a.i./ha at 6–9 day intervals for a total seasonal rate of 580–600 g a.i./ha. Mature winter squash was harvested 3–4 days after the final application.

Commodity	Total Rate (g a.i./ha)	PHI (days)	Quinoxyfen Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Winter Squash	580–600	3–4	10	0.027	0.106	0.106	0.059	0.062	0.03

FREEZER STORAGE STABILITY — **PMRA# 1641950, 1641952, 1641954**

Freezer storage stability data indicated that quinoxyfen residues are stable at -18°C for up to six months in apples, apricots, peaches, strawberries, artichokes and zucchini, and for up to 12 months in grapes.

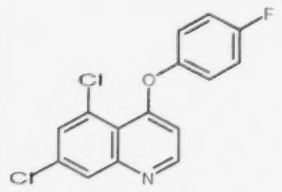
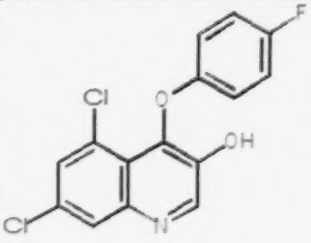
PROCESSED FOOD AND FEED — **PMRA# 779414, 941125 and 1771828**

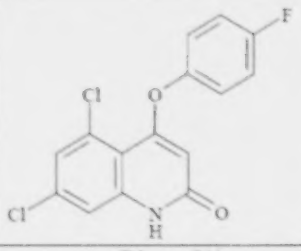
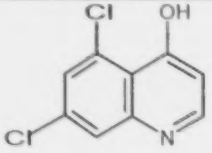
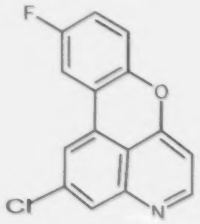
Processing studies were conducted on grapes and plums. Residues of quinoxyfen were only observed to concentrate into dried prune plums (3.5x).

Table 6 Food Residue Chemistry Overview of Metabolism Studies and Risk Assessment

PLANT STUDIES			
RESIDUE DEFINITION FOR ENFORCEMENT **Primary crops** **Rotational crops**		Quinoxyfen Quinoxyfen	
RESIDUE DEFINITION FOR RISK ASSESSMENT **Primary crops** **Rotational crops**		Quinoxyfen Quinoxyfen	
METABOLIC PROFILE IN DIVERSE CROPS		The metabolic profile is similar in five dissimilar crops.	
ANIMAL STUDIES			
RESIDUE DEFINITION FOR ENFORCEMENT		NA	
RESIDUE DEFINITION FOR RISK ASSESSMENT		NA	
METABOLIC PROFILE IN ANIMALS		Metabolic profile in animals was not investigated.	
FAT SOLUBLE RESIDUE		Not determined	
DIETARY RISK FROM FOOD AND WATER			
	POPULATION	**ESTIMATED RISK % of ACCEPTABLE DAILY INTAKE (ADI)**	
		Food Only	**Food and Water**
Basic chronic non-cancer dietary risk **ADI = 0.2 mg/kg bw/day** **Estimated chronic drinking water concentration = 0.59 µg/L**	**All infants < 1 year**	0.8	0.8
	Children 1–2 years	2.1	2.1
	Children 3 to 5 years	1.8	1.8
	Children 6–12 years	1.3	1.3
	Youth 13–19 years	1.1	1.1
	Adults 20–49 years	1.3	1.3
	Adults 50+ years	1.2	1.2
	Total population	1.3	1.3

Table 7 Identity, Maximum Formation Rate and Time of Maximum Occurrence of Transformation Products Formed in the Environment

Code	Chemical name	Chemical structure	Study	Max %AR (day)	%AR at Study End (study length)
PARENT					
XDE-795 DE-795	5,7-dichloro-4-(4-fluorophenoxy)quinoline				
MAJOR (>10%) TRANSFORMATION PRODUCTS					
	5,7-dichloro-4-(4-fluorophenoxy)quinolin-3-ol (3-OH-quinoxyfen)[1]		Aerobic soil (range for various labels , type of soils and T°)	5.8–67.5 (180–365)	2.2–67.5
			Anaerobic soil	18.25 (32)	6.0 (100)
			Soil photolysis	0 (NA)	0 (30)
			Aqueous photolysis pppphophotolysis	0 (NA)	0 (7)
			Hydrolysis	0 (NA)	0 (21)
			Aerobic aquatic (Range for 2 labels)	38.4–42.7 (48)	30.6–36.4 (100)
			Anaerobic aquatic (Range for 2 labels)	81.8–86.9 (181–378)	81.8–84.5 (378)
			Field studies	2.0 (372)	<LOD (489)
			Other:	NA	NA

Code	Chemical name	Chemical structure	Study	Max %AR (day)	%AR at Study End (study length)
	5,7-dichloro-4-(4-fluorophenoxy)-2-oxo-quinoline (2-oxo-quinoxyfen)[1]				
	5,7-dichloroquinolin-4-ol (DCHQ)		Aerobic soil (range for various labels , type of soils and T°)	0.0–20.2 (7–365)	0–20.2 (365)
			Anaerobic soil	0 (NA)	0 (100)
			Soil photolysis	2.5 (30)	2.5 (30)
			Aqueous photolysis	0 (NA)	0 (7)
			Hydrolysis (pH 4, 50°C; stable at pH 7 &9)	85 (21)	85 (21)
			Aerobic aquatic	0.9 (100)	0.9 (100)
			Anaerobic aquatic	0 (NA)	0 (378)
			Field studies	7.7 (62)	< LOD (378)
			Other:	NA	NA
	2-chloro-10-fluoro-7a,11a-dihydrochromeno[2,3,4-de]quinoline (CFBPQ)		Aerobic soil	0 (NA)	0 (365)
			Anaerobic soil	0 (NA)	0 (100)
			Soil photolysis	0 (NA)	0 (30)
			Aqueous photolysis	91.0 (0.04	1.7 (7)
			Hydrolysis	0 (NA)	0 (21)
			Aerobic aquatic	0 (NA)	0 (100)
			Anaerobic aquatic	0 (NA)	0 (378)
			Field studies	0 (NA)	0 (378)
			Other:	NA	NA

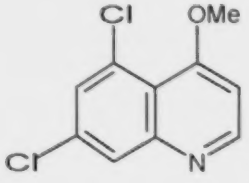
Code	Chemical name	Chemical structure	Study	Max %AR (day)	%AR at Study End (study length)
MINOR (<10%) TRANSFORMATION PRODUCTS					
	5,7-dichloro-4-methoxyquinoline (DCMQ)		Aerobic soil	0.0–3.4 (300–365)	0.0– 3.3 (365)
			Anaerobic soil	0 (NA)	0 (100)
			Soil photolysis	0 (NA)	0 (30)
			Aqueous photolysis	0 (NA)	0 (7)
			Hydrolysis	0 (NA)	0 (21)
			Aerobic aquatic	0 (NA)	0 (100)
			Anaerobic aquatic	0 (NA)	0 (378)
			Field studies	0 (NA)	0 (378)
			Other:	NA	NA

Table 8 Major Groundwater and Surface Water Model Inputs for Level 1 Assessment of Quinoxyfen and 2-oxo-quinoxyfen

Type of Input	Parameter	Value
Application Information	Crop(s) to be treated	apricots, cherries, grapes, lettuce, melons, nectarines, peaches, plums and prunes, pumpkins, squash and zucchini, strawberries and hops
	Maximum allowable application rate per year (g a.i./ha)	625 (apricots, cherries, nectarines, peaches, plums and prunes) 440 (melons, pumpkins, squash and zucchini and strawberries)
	Maximum rate each application (g a.i./ha)	125 (apricots, cherries, nectarines, peaches, plums and prunes) 110 (melons, pumpkins, squash and zucchini and strawberries)
	Maximum number of applications per year	5 (apricots, cherries, nectarines, peaches, plums and prunes) 4 (melons, pumpkins, squash and zucchini and strawberries)
	Minimum interval between applications (days)	10
	Method of application	Foliar airblast
Environmental Fate Characteristics	Hydrolysis half-life at pH 7 (days)	stable
	Photolysis half-life in water (days)	0.006
	Adsorption K_{OC} (mL/g)	45224.2 (20^{th} percentile of 5 K_{OC} values for quinoxyfen)
	Aerobic soil biotransformation half-life (days)	263 for quinoxyfen parent (longest of 2 half-lives)

Type of Input	Parameter	Value
		618 for combined residues of quinoxyfen + 2-oxo-quinoxyfen (longest of 2 half-lives)
	Aerobic aquatic biotransformation half-life (days)	33.7 for quinoxyfen parent (longest of 2 half-lives) 153 for combined residues of quinoxyfen + 2-oxo-quinoxyfen (longest of 2 half-lives)
	Anaerobic aquatic biotransformation half-life (days)	15.4 for quinoxyfen parent (only 1 half-life) 2010 for combined residues of quinoxyfen + 2-oxo-quinoxyfen (only 1 half-life)

Table 9 Level 1 Estimated Environmental Concentrations of Combined Residues of Quinoxyfen and 2-oxo-quinoxyfen in Potential Drinking Water

Compound	Groundwater EEC (μg a.i./L)		Surface Water EEC (μg a.i./L)			
			Reservoir		Dugout	
	Daily[1]	Yearly[2]	Daily[3]	Yearly[4]	Daily[3]	Yearly[4]
Combined residues (quinoxyfen + 2-oxo-quinoxyfen)	0	0	4.5	0.23	7.1	0.59

Notes:
1 90th percentile of daily average concentrations
2 90th percentile of yearly average concentrations
3 90th percentile of yearly peak concentrations
4 90th percentile of yearly average concentrations

Table 10 Fate and Behaviour in the Environment

Study	Compound	Value	Remarks	Reference
Abiotic transformation				
Hydrolysis	Quinoxyfen	pH 4 at 50, 40 and 25°C: t ½ of 6.8, 15.6 and 71.6 days pH 7 at 50°C: t ½ of 226 days pH 9 at 50°C: stable	No major degradation at relevant environmental temperatures and pHs	928643 1642957
	DCHQ	Rates of dissipation not calculable	DCHQ was identified at all temperatures and pHs tested: pH 4 at 50°C, 86.1% AR at 21 DAT; pH 4 at 40°C, 73.6% AR at 30 DAT; pH 4 at 25°C, 30.4% AR at 46 DAT pH 7 and 9 at 50°C, 3.3 and 1.0% AR at 21 DAT	

Study	Compound	Value	Remarks	Reference
Soil photolysis	Quinoxyfen	t½ 87 days in growth cabinet (equivalent to 242 days under natural spring sunlight at latitude 51°N)	Not an important route of dissipation in the environment	928656 1642958
Aqueous photolysis	Quinoxyfen	pH 5, buffered pure water: t½ 8.1 min. (environmental, 40°N latitude in spring)	Important route of dissipation in the environment	928655 1771841
	CFBPQ	SFO DT_{50} 0.2 days (continuous irradiation)	% AR 75.7–1.7 at 0.06–7 DAT	
Biotransformation				
Aerobic soil	Quinoxyfen	80th percentile (range), SFO 15°C DT_{50} 886.8 days (562–921) 25°C DT_{50} 261.2 days (116–284) 30°C DT_{50} 172.8 days (74.3–174)	Moderately persistent to persistent. Varies inversely with temperature.	928668 1642960
	2-oxo-quinoxyfen	Rates of dissipation not calculable	Max AR: 5.8–67.5% between 180–365 DAT	
	DCHQ	Rates of dissipation not calculable	Max AR: 7.0–20.2% at 240–365 DAT	
Anaerobic soil	Quinoxyfen	DT_{50} 275 days, SFO (sand/sandy loam)	Persistent	928794 1642961
	2-oxo-quinoxyfen	Rates of dissipation not calculable	18–6% AR at 32–100 DAT	
Aerobic water/ sediment (dark system)	Quinoxyfen	Total system: DT_{50} 33.7 days, SFO	Slightly persistent. Rapid dissipation in aqueous phase.	928734 1771846
	2-oxo-quinoxyfen	Rates of dissipation not calculable	0.8% AR in water, 33.5% AR in sediment at 100 DAT	
Anaerobic water/ sediment	Quinoxyfen	Total system: DT_{50} 12.7 days, SFO	Non-persistent	928673 1642963
	2-oxo-quinoxyfen	Rates of dissipation not calculable	0.3% AR in water, 83.2% AR in sediment at 378 DAT	
Adsorption/ desorption	Quinoxyfen	K_{oc} 36949–74244	Immobile	1771848 1642964
	2-oxo-quinoxyfen	K_{oc} 17400–63900	Immobile	
	DCHQ	K_{oc} 1490–8680	Low mobility to immobile	
Field dissipation	Quinoxyfen	DT_{50} 83.6 days, SFO (Ecoregion 8.1, ON)	Moderately persistent	928766 1667658
	2-oxo-quinoxyfen		0–15 cm layer: Max of 12.4 g a.i. equivalent/ha at 372 DAT and < LOD at 489 DAT 15–30 and 45–60 cm layers: 0 or < LOD g a.i. equivalent/ha at all sampling times 60–75 cm layer: Max of 11.9 g a.i. equivalent/ha at 14 DAT and 0 or < LOD at 62–372 DAT 75–90 cm layer: 0 or < LOD g a.i. equivalent/ha at all sampling times	

Study	Compound	Value	Remarks	Reference
	DCHQ		0–15 cm layer: Max of 47.5 g a.i. equivalent/ha at 62 DAT and < LOD at 372–489 DAT 15–30 cm layer: 0 g a.i. equivalent/ha at all sampling times	

Table 11 Toxicity to Non-Target Species

Test organism	Study type	Substance	Endpoint value	Reference
Terrestrial organisms				
Eisenia foetida (earthworm)	Acute	Quinoxyfen	14-d LC_{50} > 923 mg a.i./kg soil 14-d NOEC 919 mg a.i./kg soil	928106 1642970
Apis mellifera (Honey bee)	Contact	Quinoxyfen	48-h LD_{50} >100 µg a.i./bee 48-h NOEL 100 µg a.i./bee (no effect at highest dose)	928575 1771855
Colinus virginianus (Bobwhite quail)	Acute oral	Quinoxyfen	14-d LD_{50} > 2250 mg a.i./kg bw 14-d NOEL 2250 mg a.i./kg bw (no effect at highest dose)	927381 1642994
	Dietary	Quinoxyfen	LD_{50} > 2467 mg a.i./kg bw/day NOEL 439 mg a.i./kg bw/day	927383 1642995
	Dietary reproduction	Quinoxyfen	NOEL 98.3 mg a.i./kg bw/day (no effect at highest dose)	927385 1642997
Anas platyrhynchos (Mallard duck)	Acute	Quinoxyfen	5-d LD_{50} >1039 mg a.i./kg bw/day 5-d NOEL 104 mg a.i./kg bw/day	1771872 1642996
	Dietary reproduction	Quinoxyfen	NOEL 44.9 mg a.i./kg bw/day (↓ eggs hatched per hen; normal hatchlings per hen; normal hatchlings per eggs set; 14-d survivors per hen; and 14-d survivors per eggs laid)	927390 1642998
Rat	Acute oral	Quinoxyfen	LD_{50} > 5000 mg a.i./kg bw	779432-779433
		EF-1351 (53.9% a.i.)	LD_{50} > 5000 mg EP/kg bw	779338
		EF-1186 (41.3% a.i.)	LD_{50} > 2000 mg EP/kg bw	779389
	Reproduction	Quinoxyfen	Parent: NOAEL 100 mg/kg bw/day Offspring: NOAEL 20 mg/kg bw/day LOAEL 100 mg/kg bw/day (↓ pup bw (LD 0–21d); ↓ overall pup BWG (LD 21)	779453, 941098, 941100, 941102
Rabbit	Developmental	Quinoxyfen	NOAEL 80 mg/kg bw/day LOAEL 200 mg/kg bw/day	779455-779456
Vascular plants	19-d seedling emergence	EF-1295 (251 g a.i./L), 11.4 mL/L solution	EC_{25} > 553 g a.i./ha	928112 1643005
	19-d vegetative vigour		EC_{25} 410 g a.i./ha (cucumber)	

Test organism	Study type	Substance	Endpoint value	Reference
Freshwater aquatic organisms				
Daphnia magna (Water flea)	48-h acute	Quinoxyfen	EC_{50} = 0.083 mg a.i./L (based on immobilization) LC_{50} = 0.091 mg a.i./L	927432 1642974
	48-h acute	3-OH-quinoxyfen	EC_{50} > 0.5 mg TP/L (highest nominal concentration tested)	927529 1642976
	48-h acute	DCHQ	EC_{50} > 0.5 mg TP/L (highest nominal concentration tested)	1804894 1642975
	21-d chronic	Quinoxyfen	NOEC 0.0278 mg a.i./L	927592 1642977
Chironomus riparius (midge)	27-d chronic	Quinoxyfen	NOEC 0.0495 mg a.i./L (mean water column concentration) NOEC 0.746 mg a.i./kg dw sediment (mean sediment concentration)	928110 1642978
	27-d chronic	2-oxo-quinoxyfen	NOEC 0.116 mg TP/L (mean water column concentration)	1894315
Oncorhynchus mykiss (rainbow trout)	96-h acute	Quinoxyfen	LC_{50} 0.27 mg a.i./L (mort ality)	927391 1642985
	21-d chronic	Quinoxyfen	NOEC 14 µg a.i./L (lethargy, loss of equilibrium, erratic movement, melanisis and ascites)	927399 1642990
	96-h acute	2-oxo-quinoxyfen	LC_{50} > 0.0419 mg a.i./L	1861980
Lepomis macrochirus Rafinesque (Bluegill sunfish)	96-h acute	Quinoxyfen	NOEC 0.284 mg a.i./L LC_{50} > 0.284 mg a.i./L	927393 1642986
Cyprinus carpio (carp)	96-h acute	Quinoxyfen	NOEC 0.1 mg a.i./L (mortality) LC_{50} 0.41 mg a.i./L	927426 1642987
Pimephales promelas (fathead minnow)	28-d ELS	Quinoxyfen	NOEC 0.013 mg a.i./L (fish length)	927885 1642991
S. capricornutum (freshwater green algae)	5-d	Quinoxyfen	E_bC_{50} 0.0278 mg a.i./L EC_{50} 0.0268 mg a.i./L (cell density)	928120 1643001
	96-h	DCHQ	EC_{50} > 0.5 mg TP/L (highest nominal concentration tested)	928128 1642999
Anabaena flos-aquae (blue-green alga)	5-d	Quinoxyfen	EC_{50} >1.24 mg a.i./L (highest concentration tested)	928538 1643000
Navicula pelliculosa (freshwater diatom)	5-d	Quinoxyfen	E_bC_{50} = 0.0287 mg a.i./L	928539 1771876
Lemna gibba (duck weed)	14-d	Quinoxyfen	EC_{50} > 1.66 mg a.i./L (frond number)	928139 1643006
Marine aquatic species				
Americamysis bahia (mysid)	96-h acute	Quinoxyfen	LC_{50} = 0.0743 mg a.i./L	927591 1642982
Crassostrea virginica (eastern oyster) Mollusk shell deposition	96-h acute	Quinoxyfen	EC_{50} = 0.072 mg a.i./L	927590 1642983
Cyprinodon variegatus (sheepshead minnow)	96-h acute	Quinoxyfen	LC_{50} > 0.168 mg a.i./L (highest measured concentration tested)	927589 1642988
	ELS	Quinoxyfen	NOEC = 0.00409 mg a.i./L (mortality)	1642989
Skeletonema costatum (saltwater diatom)	5-d	Quinoxyfen	EC_{50} = 0.106 mg a.i./L	928142 1643003

Table 12 Endpoints Used in the Risk Assessment and the Uncertainty Factors Applied

Taxonomic group	Exposure	Endpoint	Uncertainty factor
Earthworm	Acute	LC_{50}	0.5
Bee	Acute contact	LC_{50}	1
Birds	Acute	LD_{50}	0.10
	Chronic	NOEL	1
Mammals	Acute	LD_{50}	0.10
	Chronic	NOEL	1
Non-target terrestrial plants	Acute	EC_{25}	1
Aquatic invertebrates	Acute	EC_{50}	0.5
	Chronic	NOEC	1
Fish	Acute	LC_{50}	0.10
	Chronic	NOEC	1
Amphibians	Acute	Fish LC_{50}	0.10
	Chronic	Fish NOEC	1
Algae		EC_{50}	0.5
Aquatic vascular plants		EC_{50}	0.5

Table 13 Screening Level Risk Assessment on Non-Target Terrestrial Species Other Than Birds and Mammals

Organism	Exposure	Endpoint value	EEC	RQ	Level of concern exceeded?
Invertebrates					
Earthworm	Acute	619 mg a.i./kg soil	0.273 mg/kg soil	$< 5.9 X10^{-4}$	No
Bee	Contact	>112 kg a.i./ha	0.242 kg/ha	$< 21.6 X10^{-4}$	No
Vascular plants					
Vascular plant	Acute	410 g a.i./ha	0.242 kg/ha	0.59	No

Table 14 Bird and Mammal Toxicity Data Used in Screening Level Risk Assessment

Group	Study type	Endpoint		Uncertainty factor	Value used for the Screening Level risk assessment
		Dose-based endpoint	Most sensitive value		
Birds	Acute oral	LD_{50}	> 2250 mg a.i./kg bw	0.1	225 mg a.i./kg bw
	Reproduction	NOEL	44.9 mg a.i./kg bw/day	–	44.9 mg a.i./kg bw/day
Mammals	Acute oral	LD_{50}	> 5000 mg a.i./kg bw	0.1	500 mg a.i./kg bw
	Reproduction	NOEL	20 mg a.i./kg bw/day	–	20 mg a.i./kg bw/day

Table 15 Screening Level: Estimated Daily Exposure (EDE) and Screening Level Risk Assessment for Birds and Mammals Following Multiple Applications of Quinoxyfen (5 x 125 g a.i./ha, with a 10-Day Interval) on Stone Fruits.

Organism weight (g)	FIR[a] (g dw diet/day)	Endpoint	Endpoint value (mg a.i./kg bw/day)	Feeding Guild (food item)	EDE[b] (mg a.i./kg bw/day)	RQ	Level of concern exceeded?
Birds							
20 g	5.1	Acute	225	Insectivore (small insects)	12.20	0.05	No
		Reproduction	44.9	Insectivore (small insects)	12.20	0.27	No
100g	19.9	Acute	225	Insectivore (small insects)	9.52	0.04	No
		Reproduction	44.9	Insectivore (small insects)	9.52	0.21	No
1000g	58.1	Acute	225	Herbivore (Short grass)	9.94	0.04	No
		Reproduction	44.9	Herbivore (Short grass)	9.94	0.22	No
Mammals							
15g	2.2	Acute	500	Insectivore (small insects)	7.02	0.01	No
		Reproduction	20.0	Insectivore (small insects)	7.02	0.35	No
35g	4.5	Acute	500	Herbivore (Short grass)	21.99	0.04	No
		Reproduction	20.0	Herbivore (Short grass)	21.99	**1.10**	**Yes**
1000g	68.7	Acute	500	Herbivore (Short grass)	11.75	0.02	No
		Reproduction	20.0	Herbivore (Short grass)	11.75	0.59	No

[a] Food Ingestion Rates (Nagy, 1987). For generic birds with body weight less than or equal to 200 g, the "passerine" equation was used; for generic birds with body weight greater than 200 g, the "all birds" equation was used:

Passerine Equation (body weight < or =200 g): FIR (g dry weight/day) = $0.398(\text{bw in g})^{0.850}$

All birds Equation (body weight > 200 g): FIR (g dry weight/day) = $0.648(\text{bw in g})^{0.651}$.

For mammals, the "all mammals" equation was used: FIR (g dry weight/day) = $0.235(\text{bw in g})^{0.822}$

[b] EDE = Estimated dietary exposure; is calculated using the following formula: (FIR/bw) x EEC.

At the screening level, food items representing the most conservative EEC for each size guild are used.

Table 16 Screening Level Risk Assessment on Non-Target Aquatic Species

Organism	Substance	Exposure	Endpoint value	EEC	RQ	Level of concern exceeded?
Freshwater species						
Daphnia magna	Quinoxyfen	Acute	0.0415 mg a.i./L	0.054 mg a.i./L	1.3	Yes
	Quinoxyfen	Chronic	0.0278 mg a.i./L		1.9	Yes
	2-oxo-quinoxyfen	Acute	> 0.25 mg TP/L	0.057 mg TP/L	< 0.2	No
	DCHQ	Acute	> 0.25 mg TP/L	0.038 mg TP/L	< 0.2	No
Chironomid	Quinoxyfen	Chronic	0.0495 mg a.i./L	0.054 mg a.i./L	1.1	Yes

Organism	Substance	Exposure	Endpoint value	EEC	RQ	Level of concern exceeded?
	2-oxo-quinoxyfen	Chronic	0.116 mg TP/L	0.057 mg TP/L	0.5	No
Rainbow trout	Quinoxyfen	Acute	0.027 mg a.i./L	0.054 mg a.i./L	2.0	Yes
	Quinoxyfen	Chronic	0.014 mg a.i./L		3.9	Yes
	2-oxo-quinoxyfen	Acute	> 0.00419 mg TP/L	0.057 mg TP/L	< 13.6	NA
Fathead minnow	Quinoxyfen	ELS	0.013 mg a.i./L	0.054 mg a.i./L	4.2	Yes
Amphibians (using the most sensitive fish endpoint as surrogate data)	Quinoxyfen	ELS	0.013 mg a.i./L	0.288 mg a.i./L	22.2	Yes
		Acute	0.027 mg a.i./L		10.7	Yes
	2-oxo-quinoxyfen	Acute	> 0.00419 mg TP/L	0.302 mg TP/L	< 72.1	NA
Freshwater green algae (*S. capricornutum*)	Quinoxyfen		0.0134 mg a.i./L	0.054 mg a.i./L	4.0	Yes
	DCHQ		> 0.25 mg TP/L	0.038 mg TP/L	< 0.15	No
Blue-green algae (*A. flos-aquae*)	Quinoxyfen		> 0.62 mg a.i./L	0.054 mg a.i./L	0.09	No
Diatom (*N. pelliculosa*)	Quinoxyfen		0.014 mg a.i./L	0.054 mg a.i./L	3.8	Yes
Vascular plant (*L. gibba*)	Quinoxyfen	Acute	> 0.83 mg a.i./L (14 d)	0.054 mg a.i./L	< 0.07	No
Marine species						
Mollusk	Quinoxyfen	Acute	0.036 mg a.i./L	0.054 mg a.i./L	1.5	Yes
Sheepshead minnow (*Cyprinodon variegatus*)	Quinoxyfen	Acute	> 0.0168 mg a.i./L		< 3.2	NA
	Quinoxyfen	ELS	0.00409 mg a.i./L		13.2	Yes
Marine algae	Quinoxyfen	Acute	0.053 mg a.i./L		1.0	Yes

Table 17 Refined Risk Assessment from Spray Drift on Non-Target Species

Organism (exposure)	Endpoint (mg a.i./L)	Refined EEC (mg a.i./L)	RQ	Level of concern exceeded?
Quinoxyfen on freshwater organisms				
Amphibians	NOEC: 0.013 mg a.i./L	Early Season Airblast (74% drift): 0.213	16.4	Yes
		Late Season Airblast (59% drift): 0.170	13.1	Yes
		Ground boom sprayer (medium) (6% drift): 0.017	1.3	Yes
Daphnia magna	NOEC: 0.0278 mg a.i./L	Early Season Airblast (74% drift): 0.040	1.4	Yes
		Late Season Airblast (59% drift): 0.032	1.1	Yes
		Ground boom sprayer (medium) (6% drift): 0.003	0.1	No
Chironomid	NOEC: 0.0495 mg a.i./L	Early Season Airblast (74% drift): 0.040	0.8	No
		Late Season Airblast (59% drift): 0.032	0.6	No
		Ground boom sprayer (medium) (6% drift): 0.003	0.1	No
Fathead minnow (28-d ELS)	NOEC: 0.013 mg a.i./L	Early Season Airblast (74% drift): 0.040	3.1	Yes
		Late Season Airblast (59% drift): 0.032	2.5	Yes
		Ground boom sprayer (medium) (6% drift): 0.003	0.2	No
Rainbow trout	NOEC: 0.014 mg a.i./L	Early Season Airblast (74% drift): 0.040	2.9	Yes
		Late Season Airblast (59% drift): 0.032	2.3	Yes
		Ground boom sprayer (medium) (6% drift): 0.003	0.2	No

Organism (exposure)	Endpoint (mg a.i./L)	Refined EEC (mg a.i./L)	RQ	Level of concern exceeded?
Green Algae	LC_{50}/2: 0.0134 mg a.i./L	Early Season Airblast (74% drift): 0.040	3.0	Yes
		Late Season Airblast (59% drift): 0.032	2.4	Yes
		Ground boom sprayer (medium) (6% drift): 0.003	0.2	No
2-oxo-quinoxyfen on freshwater organisms				
Rainbow trout	LC_{50}/10: > 0.00419 mg TP/L	Early Season Airblast (74% drift): 0.042	< 10.1	NA
		Late Season Airblast (59% drift): 0.034	< 8.0	NA
		Ground boom sprayer (medium) (6% drift): 0.003	< 0.8	No
Amphibians	LC_{50}/10: > 0.00419 mg TP/L	Early Season Airblast (74% drift): 0.223	< 53.3	NA
		Late Season Airblast (59% drift): 0.178	< 42.5	NA
		Ground boom sprayer (medium) (6% drift): 0.018	< 4.3	NA
		Late Season Airblast (59% drift): 0.034	< 1.3	NA
		Ground boom sprayer (medium) (6% drift): 0.003	< 0.1	No
Quinoxyfen on marine organisms				
Sheephead minnow (39-d ELS)	NOEC: 0.00409 mg a.i./L	Early Season Airblast (74% drift): 0.040	9.8	Yes
		Late Season Airblast (59% drift): 0.032	7.8	Yes
		Ground boom sprayer (medium) (6% drift): 0.003	0.7	No
Eastern Oyster	LC_{50}/2: 0.036 mg a.i./L	Early Season Airblast (74% drift): 0.040	1.1	Yes
		Late Season Airblast (59% drift): 0.032	0.9	No

Organism (exposure)	Endpoint (mg a.i./L)	Refined EEC (mg a.i./L)	RQ	Level of concern exceeded?
		Ground boom sprayer (medium) (6% drift): 0.003	0.1	No
Saltwater diatom	LC_{50}/2: 0.053 mg a.i./L	Early Season Airblast (74% drift): 0.040	0.8	No
		Late Season Airblast (59% drift): 0.032	0.6	No
		Ground boom sprayer (medium) (6% drift): 0.003	0.1	No

Table 18 Refined Risk Assessment from Predicted Runoff of Quinoxyfen on Non-Target Species

Organism (exposure)	Endpoint (µg a.i./L)	EEC (µg a.i./L)	RQ	Level of concern exceeded?
Daphnia magna	NOEC: 27.8	3.3 (Prairie Region)	0.1	No
Amphibians	NOEC: 13.0	18.0 (Prairie Region)	1.4	Yes
Fathead minnow (28-d ELS)	NOEC: 13.0	3.3 (Prairie Region)	0.3	No
Green algae	LC_{50}/2: 13.4	3.3 (Prairie Region)	0.2	No
Eastern Oyster	LC_{50}/2: 36.0	2.6 (Atlantic Region)	0.1	No
Sheephead minnow (39-d ELS)	NOEC: 4.1	2.6 (Atlantic Region)	0.6	No
Saltwater diatom	LC_{50}/2: 53.0	2.6 (Atlantic Region)	0.0	No

Table 19 Toxic Substances Management Policy (TSMP) Considerations – Comparison to Toxic Substances Management Policy

TSMP Track 1 Criteria	TSMP Track 1 Criterion value		Quinoxyfen Endpoints
CEPA toxic or CEPA toxic equivalent[1]	Yes		Yes
Predominantly anthropogenic[2]	Yes		Yes
Persistence[3]:	**Soil - Laboratory**	Half-life ≥ 182 days	Half-life (days), 80th percentile and range at: 15°C 886.8 (562–921) 25°C 261.2 (116–284) 30°C 172.8 (74.3–174)
	Soil – Field		Half-life (days) 83.6

TSMP Track 1 Criteria	TSMP Track 1 Criterion value		Quinoxyfen Endpoints
			Carryover 15.2% At least 37% of the soil concentration measured after the application remained at the end of the season.
	Water	Half-life ≥ 182 days	Half-life in total system 33.7 days (aerobic) 12.7 days (anaerobic)
	Sediment	Half-life ≥ 365 days	Half-life 35.3 days (aerobic) 12.6 days (anaerobic)
	Air Not likely	Half-life ≥ 2 days or evidence of long range transport	Half-life 1.88 day Volatilisation would not be an important route of dissipation and long-range atmospheric transport is unlikely to occur based on the vapour pressure (1.2×10^{-5} Pa) and Henry's Law Constant (3.187×10^{-2} Pa m^3/mole). $1/H = 7.64 \times 10^4$, indicating a slight volatility from a water surface. Not detected in Sweden in 2006 (preliminary review of a monitoring study)
Bioaccumulation[4]	Log $K_{ow} \geq 5$ No		4.66
	BCF ≥ 5000 Yes		5040 for fish Residues in whole fish: Steady state (14 days): 2002 µg/kg whole fish 14-day depuration: 192 µg/kg whole fish
	BAF ≥ 5000 Not likely		Earthworms: estimations[5] of up to 13 Aquatic organisms: only low levels were detected in biota in a field study (up to 6.69 µg a.i./kg fw in fish)
Is the chemical a TSMP Track 1 substance (all four criteria must be met)?			Not likely

[1] All pesticides will be considered CEPA-toxic or CEPA toxic equivalent for the purpose of initially assessing a pesticide against the TSMP criteria. Assessment of the CEPA toxicity criteria may be refined if required (i.e., all other TSMP criteria are met).

[2] The policy considers a substance "predominantly anthropogenic" if, based on expert judgement, its concentration in the environment medium is largely due to human activity, rather than to natural sources or releases.

[3] If the pesticide and/or the transformation product(s) meet one persistence criterion identified for one media (soil, water, sediment or air) than the criterion for persistence is considered to be met.

[4] Field data (for example, BAFs) are preferred over laboratory data (for example, BCFs) which, in turn, are preferred over chemical properties (for example, log K_{ow}).

[5] BAF values were recalculated with appropriate ratios and estimated based on a range of potential earthworm weight on a dry weight basis since the studies only provided earthworm weights on a fresh weight basis.

Table 20 List of Active Ingredients Currently Registered on Grape, Melons, Pumkin, Winter Squash, Head and Leaf Lettuce, Stone Fruits, Strawberry and Hops

Crop	Pathogen	Fungicide Active Ingredients
Grape	*Uncinula necator*	• Sulfur • Phosalone + Ferbam • Copper • *Bacillus subtilis* • Potassium bicarbonate • Myclobutanil
Melons, pumkin, and winter squash	*Sphaerotheca fuliginea*	• Copper • Chlorothalonil • Metiram • Boscalid • *Bacillus subtilis* • Potassium bicarbonate
Head and leaf lettuce	*Erysiphe cichoracearum*	• *Bacillus subtilis*
Stone fruits		• Potassium bicarbonate • Myclobutanil
Strawberry	*Sphaerotheca macularis*	• Boscalid • Boscalid + Pyraclostrobin • Cupper • Myclobutanil • *Streptomyces lydicus* strain WYEC 108
Hops	*Sphaerotheca macularis*	• None

Table 21 Use (Label) Claims Proposed by Applicant and Whether Acceptable or Unsupported

Proposed Claims	Supported Claims
Grape: Control of powdery mildew caused by *Uncinula necator* with Quintec Fungicide at the rate of **300–480** mL product /ha. Repeat applications at 14 day intervals, maximum of five applications.	**Grape:** Control of powdery mildew caused by *Uncinula necator* with five applications of Quintec Fungicide at the rate of **300** mL product /ha. Repeat applications at 14 day intervals, maximum of five applications.
Melons, pumpkin, winter squash: Control of powdery mildew caused by *Sphaerotheca fuliginea* with Quintec Fungicide at the rate of **300–440** mL product /ha. Repeat applications at 10–14 day intervals, maximum of four applications.	**Melons, pumpkin, winter squash**: Supported as proposed.
Head and leaf lettuce: Control of powdery mildew caused by *Erysiphe cichoracearum* with Quintec Fungicide at the rate of **300–440** mL product /ha. Repeat applications at 10–14 day intervals, maximum of five applications.	**Head and leaf lettuce:** Control of powdery mildew caused by *Erysiphe cichoracearum* with four applications of Quintec Fungicide at the rate of **240** mL product /ha. Repeat applications at 10–14 day intervals, maximum of five applications.

Proposed Claims	Supported Claims
Stone fruit : Control of powdery mildew caused by *Podosphaera clandestina* with Quintec Fungicide at the rate of **500** mL product /ha. Repeat applications at 10–14 day intervals, maximum of five applications.	**Stone fruit** : Control of powdery mildew caused by *Podosphaera clandestina* with five applications of Quintec Fungicide at the rate of **500** mL product /ha. Suppression of powdery mildew caused by *Sphaerotheca pannosa* with five applications of Quintec Fungicide at the rate of **500** mL product /ha. Repeat applications at 10–14 day intervals, maximum of five applications.
Strawberry: Control of powdery mildew caused by *Sphaerotheca macularis* with Quintec Fungicide at the rate of 300–440 mL product /ha. Repeat applications at 10–14 day intervals, maximum of four applications.	**Strawberry:** Supported as proposed.
Hops: Control of powdery mildew caused by *Sphaerotheca macularis* with four applications of Quintec Fungicide at the rate of 300–500 mL product /ha. Repeat applications at 14 day intervals, maximum of four applications.	**Hops:** Control of powdery mildew caused by *Sphaerotheca macularis* with Quintec Fungicide at the rate of 300–500 mL product /ha. Apply a maximum of two applications. Repeat applications at 14 day intervals, maximum of four applications.

Appendix II Supplemental Maximum Residue Limit Information – International Situation and Trade Implications

All specified Canadian MRLs are the same as the tolerances established in the United States (40 CFR Part 180), but differ from the established Codex MRLs.

Table 1 Differences Between MRLs in Canada and in Other Jurisdictions

Commodity	Canada (ppm)	United States (ppm)	Codex* (ppm)
Leaf lettuce	19.0	19.0	20
Head lettuce	7.0	7.0	8
Strawberries	0.9	0.90	1
Crop Group 12-09 (Stone Fruits)	0.7	0.70 (Tolerances established for Fruit, stone, group 12)	0.4 (for cherries); other stone fruits not reviewed by Codex
Winter squash, pumpkins	0.2	0.20	Not included in Codex
Crop Subgroup 9A (Cucurbit Vegetables - Melon Subgroup)	0.08	0.08	0.1 (for melons, except watermelon)

* Codex is an international organization under the auspices of the United Nations that develops international food standards, including MRLs.

MRLs may vary from one country to another for a number of reasons, including differences in pesticide use patterns and the locations of the field crop trials used to generate residue chemistry data. For animal commodities, differences in MRLs can be due to different livestock feed items and practices.

Under the North American Free Trade Agreement (NAFTA), Canada, the United States and Mexico are committed to resolving MRL discrepancies to the broadest extent possible. Harmonization will standardize the protection of human health across North America and promote the free trade of safe food products. Until harmonization is achieved, the Canadian MRLs specified in this document are necessary. The differences in MRLs outlined above are not expected to impact businesses negatively or adversely affect international competitiveness of Canadian firms or to negatively affect any regions of Canada.

Appendix III Crop Groups: Numbers and Definitions

Crop Group Number	Name of the Crop Group	Commodity
9A	Cucurbit Vegetable Group – Melon Subgroup	Citron melons, cantaloupes, muskmelons (other than those listed in this item), watermelons
12-09	Stone Fruits	Apricots, sweet cherries, tart cherries, nectarines, peaches, plums, Chickasaw plums, Damson plums, Japanese plums, plumcots, fresh prune plums, Japanese apricots, capulins, black cherries, Nanking cherries, chokecherries, American plums, beach plums, Canada plums, cherry plums, Klamath plums, sloes

References

A. List of Studies/Information Submitted by Registrant

1.0 Chemistry

PMRA Document Number	Reference
779425	2001, Group A: Product Identity and Composition, Description of Materials Used to Produce the Product, Description of Production Process. Discussion of the Formation of Impurities, Certified Limits, Preliminary Analysis, Enforcement Analytical Method, and Submittal of Samples of Quinoxyfen Technical, DACO 2.11.1, 2.11.2, 2.11.3, 2.11.4, 2.12.1, 2.12.2, 2.13.1, 2.13.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9 CBI
779429	2000, Group B: Physical and Chemical Properties of Quinoxyfen (DE-795) and Supplemental Properties of 3-Hydroxy XDE-795, DACO: 2.14.1, 2.14.10, 2.14.11, 2.14.12, 2.14.13, 2.14.14, 2.14.2, 2.14.3, 2.14.4, 2.14.5, 2.14.6, 2.14.7, 2.14.8, 2.14.9 CBI
779430	2002, Storage Stability and Package Corrosion Characteristics of Quinoxyfen Technical; One Year Study, DACO: 2.14.14 CBI
1134782	2003, Analysis of Product Samples for the Active Ingredient and Impurities in Quinoxyfen Technical - Summary and Confidential Attachment, DACO: 2.13.1, 2.13.2, 2.13.3 CBI
1134807	2003, Correspondence - Analysis of Product Samples for the Active Ingredient and Impurities in Quinoxyfen Technical, DACO: 2.13.1,2.13.2,2.13.3 CBI
1642947	1995, (EPA 86-5) Determination of XDE-795 and 3-Hydroxy Metabolite Residues in Soil, DACO: 8.2.2,8.2.2.1
1642948	2001, Method Validation Report for the Determination of XDE-795 (Quinoxyfen) and the 3-Hydroxyl Metabolite Residues in Soil Using DAS Method ERC 94.27, DACO: 8.2.2,8.2.2.1
1642949	1995, (EPA 86-5) Independent Validation Method of DowElanco Method ERC 94.27 for the Determination of XDE-795 and its 3-Hydroxy Metabolite in Soil, DACO: 8.2.2,8.2.2.1
1642950	1995, Method Validation Report for the Determination of Quinoxyfen and its Metabolites in Soil by GC with Tandem Mass Spectrometry Detection using DAS Method GRM 00.16, DACO: 8.2.2,8.2.2.1
1642951	2008, 8.2.2 Sediment, DACO: 8.2.2.2
1642952	1995, (EPA 86-5) Determination of XDE-795 in Drinking Water, DACO: 8.2.2.3
1642953	1995, Determination of XDE-795 and DCHQ Residues in Surface Water, DACO: 8.2.2.3
1642955	1995, Validation of Analytical Methods for Use for the Determination of XDE-795 Technical Concentrations during Aquatic Toxicity Studies, DACO: 8.2.2.4
1771804	2002, Validation of Analytical Method DAS-AM-02-001 for the Determination of the Active Ingredient and Related Impurities in Technical Grade Quinoxyfen [5,7-dichloro-4-(4-fluorophenoxy)quinoline], DACO: 2.13.1 CBI
1771805	2003, Analytical Method and Validation for Determination of Sulfolane in Quinoxyfen Technical, DACO: 2.13.1 CBI
1771806	2008, Specificity of Analytical Method DAS-AM-02-001 for the Determination of Impurities in Quinoxyfen Technical, DACO: 2.13.1 CBI
779380	2001, Group A - Product Identity, Composition, and Analysis for Quinoxyfen End-Use Product (EF-1295), DACO 3.2, 3.3.1, 3.4.1 CBI

779383	2000, Group B: Determination of Color, Physical State, Odor, Oxidizing and Reducing Action, Flammability, Explodability, pH, Viscosity and Density of EF-1295, a Liquid End Use Product containing Quinoxyfen DACO: 3.5.1, 3.5.11, 3.5.12, 3.5.13, 3.5.14, 3.5.15, 3.5.2, 3.5.3, 3.5.4, 3.5.5, 3.5.6, 3.5.7, 3.5.8, 3.5.9 CBI
779384	2000, Group B - Physical/Chemical Properties for EF-1295, a Liquid End-Use Products Containing Quinoxyfen, DACO 3.5.1, 3.5.2, 3.5.3, 3.5.4, 3.5.6, 3.5.7, 3.5.8, 3.5.9, 3.5.11, 3.5.12, 3.5.13, 3.5.14, 3.5.15 CBI
779386	1999, (EPA 86-5) Packaging Storage Stability Trial for Quinoxyfen 250 g/L SC, DACO 3.5.5, 3.5.10 CBI
1771815	2009, 090607 Detailed Description of Quintec SC (EF-1295) from Technical Material, DACO: 3.2.2 CBI

2.0 Human and Animal Health

PMRA Document Number	Reference
779432	1994, XDE-795: Acute Oral Toxicity Study in Fischer 344 Rats, DACO: 4.2.1
779433	2001, Supplemental Report for: XDE-795: Acute Oral Toxicity Study in Fischer 344 Rats. Comments: Summary & Appendix Table 1, DACO: 4.2.1
779434	1994, XDE-795: Acute Dermal Toxicity Study in New Zealand White Rabbits, DACO: 4.2.2
779435	1994, XDE-795: Acute Aerosol Inhalation Toxicity Study with Fischer 344 Rats, DACO: 4.2.3
779436	1994, XDE-795: Primary Eye Irritation Study in New Zealand White Rabbits, DACO: 4.2.4
779437	1994, XDE-795: Primary Dermal Irritation Study in New Zealand White Rabbits, DACO: 4.2.5
779438	1994, XDE-795: Dermal Sensitization Potential in the Hartley Albino Guinea Pig, DACO: 4.2.6
779439	1995, XDE-795 Technical: Delayed Contact Hypersensitivity Study in the Guinea Pig, DACO: 4.2.6
779440	1992, XR-795: 13-Week Dietary Toxicity Study in CD-1 Mice, DACO: 4.3.1
779441	2002, Supplemental Report for: XR-795: 13- Week Dietary Toxicity Study in CD-1 Mice, DACO: 4.3.1
779442	1992, 13-Week Dietary Toxicity Study with 4- Week Study in Fischer 344 Rats, DACO: 4.3.1
779443	2001, Supplemental Report for: 13-Week Dietary Toxicity Study with 4-Week Study in Fischer 344 Rats, DACO: 4.3.1
779444	1992, XR-795: Four-Week Dietary Toxicity Study in Fischer 344 Rats, DACO: 4.3.1
779445	1992, XR-795: Palatability and Toxicity Probe Study in Beagle Dogs, DACO: 4.3.2
779446	1993, XR-795: Four-Week Dietary Toxicity Study in Beagle Dogs, DACO: 4.3.2
779447	1992, 13-Week Dietary Toxicity Study in Beagle Dogs, DACO: 4.3.2
779448	2001, Supplemental Report for: 13-Week Dietary Toxicity Study in Beagle Dogs, DACO: 4.3.2

779449	1995, XDE-795: One-Year Chronic Dietary Toxicity Study in Beagle Dogs, DACO: 4.3.2
779450	2000, Quinoxyfen: 4-Week Dermal Toxicity Study in Fischer 344 Rats, DACO: 4.3.5
779451	1995, XDE-795: Two-Year Dietary Chronic Toxicity/Oncogenicity Study in Fischer 344 Rats, DACO: 4.4.1,4.4.4
779452	1995, XDE-795: Potential Tumourigenic Effects in Prolonged Dietary Administration to CD-1 Mice, DACO: 4.4.3
779453	1995, XDE-795: Two-Generation Dietary Reproduction Study in Sprague-Dawley Rats, DACO: 4.5.1
779454	1994, XDE-795: A Study of the Effect on Pregnancy of the Rat, DACO: 4.5.2
779455	1993, XDE-795: Oral Gavage Teratology Probe Study in New Zealand White Rabbits, DACO: 4.5.3
779456	1994, XDE-795: Oral Gavage Teratology Study in New Zealand White Rabbits, DACO: 4.5.3
779457	1994, XDE-795: Test for Chemical Induction of Gene Mutation at the HGPRT Locus in Cultured Chinese Hamster Ovary (CHO) Cells with Metabolic Activation, DACO: 4.5.5
779458	1994, Evaluation of CDE-795 in an in-vitro Chromosomal Aberration Assay Utilizing Rat Lymphocytes, DACO: 4.5.6
779459	1994, Evaluation of XDE-795 in the Mouse Bone Marrow Micronucleus Test, DACO: 4.5.7
779460	2001, Supplemental Report for: Evaluation of XDE-795 in the Mouse Bone Marrow Micronucleus Test, DACO: 4.5.7
779461	1993, Evaluation of XR-795 in the Salmonella typhimurium Preincubation Mutation Assay in the Presence and Absence of Aroclor-Induced Liver S-9 with a Confirmatory Study, DACO: 4.5.8
779462	1995, XDE-795: Tissue Distribution and Metabolism of 14C-Labelled XDE-795 in Fischer 344 Rats, DACO: 4.5.9
779463	2001, Quinoxyfen (DE-795): Determination of Hydroxylated Metabolites of Quinoxyfen Following a Repeated Oral Administration in Fischer 344 Rats, DACO: 4.5.9
779464	1999, Quinoxyfen: Acute Neurotoxicity Study in Fischer 344 Rats, DACO: 4.5.10
779465	1995, XDE-795: Chronic Neurotoxicity Study in Fischer 344 Rats, DACO: 4.5.11
940756	1995, XDE-795: One-Year Chronic Dietary Toxicity Study in Beagle Dogs, DACO: 4.3.2
940762	2000, Quinoxyfen: 4-Week Dermal Toxicity Study in Fischer 344 Rats, DACO: 4.3.5
940780	1995, XDE-795: Two-Year Dietary Chronic Toxicity/Oncogenicity Study in Fischer 344 Rats - Final Report, DACO: 4.4.1,4.4.4
940782	1995, XDE-795: Two-Year Dietary Chronic Toxicity/Oncogenicity Study in Fischer 344 Rats - Final Report, DACO: 4.4.1,4.4.4
940784	1995, XDE-795: Two-Year Dietary Chronic Toxicity/Oncogenicity Study in Fischer 344 Rats - Final Report, DACO: 4.4.1,4.4.4
940786	1995, XDE-795: Two-Year Dietary Chronic Toxicity/Oncogenicity Study in Fischer 344 Rats - Final Report, DACO: 4.4.1,4.4.4
940788	1995, XDE-795: Two-Year Dietary Chronic Toxicity/Oncogenicity Study in Fischer 344 Rats - Final Report, DACO: 4.4.1,4.4.4

940790	1995, XDE-795: Two-Year Dietary Chronic Toxicity/Oncogenicity Study in Fischer 344 Rats - Final Report, DACO: 4.4.1,4.4.4
940792	1995, XDE-795: Two-Year Dietary Chronic Toxicity/Oncogenicity Study in Fischer 344 Rats - Final Report, DACO: 4.4.1,4.4.4
940801	2001, XDE-795: Two-Year Dietary Chronic Toxicity/Oncogenicity Study in Fischer 344 Rats - Final Report, DACO: 4.4.1,4.4.4
940806	1995, XDE-795: Potential Tumourigenic Effects in Prolonged Dietary Administration to CD-1 Mice, DACO: 4.4.3
940808	1995, XDE-795: Potential Tumourigenic Effects in Prolonged Dietary Administration to CD-1 Mice, DACO: 4.4.3
940897	1995, XDE-795: Potential Tumourigenic Effects in Prolonged Dietary Administration to CD-1 Mice, DACO: 4.4.3
940899	1995, XDE-795: Potential Tumourigenic Effects in Prolonged Dietary Administration to CD-1 Mice, DACO: 4.4.3
941098	1995, XDE-795: Two-Generation Dietary Reproduction Study in Sprague-Dawley Rats, DACO: 4.5.1
941100	1995, XDE-795: Two-Generation Dietary Reproduction Study in Sprague-Dawley Rats, DACO: 4.5.1
941102	1995, XDE-795: Two-Generation Dietary Reproduction Study in Sprague-Dawley Rats, DACO: 4.5.1
941108	1999, Quinoxyfen: Acute Neurotoxicity Study in Fischer 344 Rats, DACO: 4.5.10
941110	1999, Quinoxyfen: Acute Neurotoxicity Study in Fischer 344 Rats, DACO: 4.5.10
941112	1995, XDE-795: Chronic Neurotoxicity Study in Fischer 344 Rats, DACO: 4.5.11
779388	2001, EF-1351: An Acute Oral Toxicity Study in Fischer 344 Rats 000264 GLP, Unpublished, DACO: 4.6.1
779389	1993, EF 1186 (XDE 795 SC): Acute Oral Toxicity Study in the Rat GHE-T-356 GLP, Unpublished, DACO: 4.6.1
779390	2001, EF-1351: An Acute Dermal Toxicity Study in Fischer 344 Rats 000265 GLP, Unpublished, DACO: 4.6.2
779392	1993, EF 1186 (XDE 795 SC): Acute Dermal Irritation Test in the Rabbit GHE-T-336 GLP, Unpublished, DACO: 4.6.2
779393	2001, EF-1351: Justification for Waiver of Acute Inhalation Study GH-C 5189 GLP, Unpublished, DACO: 4.6.3
779394	2001, EF-1186: Justification for Waiver of Acute Inhalation Study GH-C 5188 GLP, Unpublished, DACO: 4.6.3
779395	1993, EF 1186 (XDE 795 SC): Acute Eye Irritation Test in the Rabbit GHE-T-368 GLP, Unpublished, DACO: 4.6.4
779396	2001, EF-1351: A Primary Eye Irritation Study in New Zealand White Rabbits 000267 GLP, Unpublished, DACO: 4.6.4
779397	2001, EF-1351: A Primary Skin Irritation Study in New Zealand White Rabbits 000266 GLP, Unpublished, DACO: 4.6.5

779398	1993, EF 1186 (XDE 795 SC): Delayed Contact Hypersensitivity Study in Guinea Pigs GHE-T-369 GLP, Unpublished, DACO: 4.6.6
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